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Increased Use of Noninvasive Ventilation Associated With Decreased Use of Invasive Devices in Children With Bronchiolitis

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Objective: To assess how a change in practice to more frequent use of high-flow nasal cannula for the treatment of bronchiolitis would affect the use of invasive devices in children.

Design: Retrospective cohort study of children under 2 years old admitted to the ICU with respiratory failure secondary to bronchiolitis. Outcomes and invasive device use were compared between two time periods, before and after the practice change.

Setting: Eighteen bed tertiary care PICU.

Patients: A total of 325 children: 146 from 2010 to 2012 and 179 from 2015 to 2016.

Interventions: None.

Measurements and Main Results: There were no significant differences between the two time periods regarding gender, race/ethnicity, medical history, and viral profile, although children were younger in the earlier cohort (median age of 1.9 mo [interquartile range, 1.2–3.5] vs 3.3 mo [1.7–8.6]; $p < 0.001$). There was an increased use of noninvasive ventilation in the second time period (94% from 69%; $p < 0.001$), as well

as a decreased frequency of intubation (13% from 42%; $p < 0.001$) and reduced central venous catheter placement (7% from 37%; $p < 0.001$). There was no significant difference in mortality between the two groups. A logistic regression analysis was conducted, which found that time period, intubation, and hospital length of stay were all independently associated with central venous catheter placement.

Conclusions: A practice change toward managing patients with bronchiolitis in respiratory failure with less invasive means was associated with a reduction in the use of other invasive devices. In our cohort, minimizing the use of invasive ventilation and devices was not associated with an increase in mortality and could potentially have additional benefits.

Key Words: bronchiolitis; noninvasive ventilation; pediatrics; resource utilization

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The authors have disclosed that they do not have any potential conflicts of interest.

Dr. Soshnick conceptualized and designed the study, collected the data, drafted the initial manuscript, and approved the final manuscript as submitted. Dr. Carroll conceptualized and designed the study, carried out the initial analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted. Dr. Cowl conceptualized and designed the study, coordinated and supervised data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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Crit Care Expl 2019; XXX:e0026

DOI: 10.1097/CCE.000000000000026

Bronchiolitis is the most common lower respiratory tract infection in infants and children worldwide (1). Respiratory syncytial virus is responsible for approximately 60% of bronchiolitis cases in children, but many different viruses can cause the same clinical presentation (1, 2). The majority of patients can be managed supportively in an outpatient setting or general inpatient unit (3), but approximately 8–13% of children with bronchiolitis progress to respiratory failure and require ICU management (4–9).

What Is Known on This Subject

Bronchiolitis is a common lower respiratory tract illness in young children, and approximately 10% of children with bronchiolitis progress to respiratory failure. These children are at risk for needing noninvasive positive-pressure ventilation, intubation, and placement of other invasive devices.

What This Study Adds

This study supports that in children with respiratory failure secondary to bronchiolitis, minimizing the use of invasive ventilation can be associated with decreased invasive device use and is not associated with an increase in mortality.

Respiratory failure in this population commonly requires intubation and may also require placement of invasive devices. These devices have both inherent risks and associated complications that can lead to prolonged hospitalizations (10, 11). There is evidence that in general, patients who have longer stays in the ICU frequently need more stable IV access in the form of indwelling central venous catheters (CVCs) (10, 11). They also can have arterial catheters and Foley catheters placed to allow for close and accurate monitoring. Patients with viral bronchiolitis are increasingly being treated with noninvasive ventilatory support via nasal/facial interfaces.

In 2012–2013, we conducted a study with other children's hospitals in the Northeast United States and compared treatment practices and outcomes in children with bronchiolitis admitted to four regional PICUs between July 2009 and July 2011 (12). Despite similar mortality risk scores among ICUs, there was considerable variation in the management of children with acute respiratory failure, including a greater than 3.5-fold increased risk of intubation between two children's hospitals (12). This may have been due to a different patient population but may also have been due to different practice patterns.

As a result of this trial, we changed our practice at Connecticut Children's Medical Center (CCMC) between 2013 and 2014. The institution invested in more devices capable of delivering noninvasive positive pressure via high-flow nasal cannula (HFNC), and we started implementing it as a type of first-line respiratory support in patients with bronchiolitis. Others have found the use of HFNC feasible in children with respiratory failure from various causes including viral bronchiolitis (9, 13), and that HFNC can decrease inspiratory effort and respiratory rate (14, 15), and may potentially decrease intubation rates (16–18).

With this practice change, we sought to assess whether the increased use of noninvasive positive pressure was associated with decreased use of other invasive devices. Specifically, we sought to compare treatment practices between two study periods (before and after our practice change), including the use of noninvasive positive pressure and the frequency of placement of certain invasive devices such as CVCs, endotracheal tubes, arterial catheters, and Foley catheters.

MATERIALS AND METHODS

A retrospective cohort study was conducted that included all children under 2 years old admitted to the CCMC ICU with acute respiratory failure secondary to viral bronchiolitis. Infants who required more than 2 L/min of oxygen and children who required over 6 L/min of oxygen were considered to be in respiratory failure. Outcomes, invasive device use, and ICU and hospital length of stay were compared between two time periods (January 1, 2010, to December 31, 2012, and January 1, 2015, to December 31, 2016), before and after a practice change toward using more HFNC respiratory support. A gap between the two time periods was chosen to exclude the timeframe of the previous study and practice change. Acute respiratory failure was diagnosed by the admitting critical care attending at admission to the ICU. Children were excluded if they were admitted outside the two study time periods. Institutional Review Board approval was granted by

CCMC in Hartford, CT, and the need for informed consent was waived. Initially, we queried the Virtual PICU Systems database (Virtual PICU Systems; LLC, Los Angeles, CA), a national quality database in which Connecticut Children's critical care division participates, to identify subjects who met our inclusion criteria. Subjects then underwent subsequent electronic medical record chart review.

Noninvasive ventilation was delivered by the Fisher & Paykel Healthcare Optiflow junior HFNC (Auckland, New Zealand) and B&B Medical Technologies bubble bottle nasal continuous positive airway pressure (NCPAP) setup (Carlsbad, CA). Per hospital protocol, all patients who receive a form of noninvasive ventilation were admitted to the PICU.

Data were analyzed using JMP statistical software (version 12.0.0; SAS Institute, Cary, NC) and using consultation from statisticians at CCMC. The relationships between time period and the baseline characteristics and clinical outcomes were compared using appropriate parametric and nonparametric tests and statistics including chi-square for dichotomous variables and Wilcoxon rank sum for continuous variables. The Kolmogorov-Smirnov statistic and the Shapiro-Wilk test were used to assess the normality of continuous variables. Data are presented as median and 25–75% interquartile range (IQR) for nonparametric continuous variables and as frequencies (%) for categorical variables. Frequencies are rounded to the nearest whole number and *p* values of less than 0.05 are considered statistically significant. Odds ratios and 95% CIs are reported where appropriate. A stepwise multiple logistic regression was performed to determine the factors associated with CVC placement using factors found significant (*p* < 0.1) on univariate analysis and reported using American College of Chest Physicians guidelines (19).

RESULTS

In 2015–2016, there were 190 children admitted to the ICU with bronchiolitis, 179 who met the study criteria. In 2010–2012, there were initially 182 children admitted to the CCMC ICU with bronchiolitis, 146 of whom met inclusion criteria. We chose a longer time period for the earlier time frame to have comparable sample sizes. Our total cohort consisted of 325 subjects. Demographic data were compared between the two time periods (**Table 1**). There was no significant difference between groups regarding gender, race/ethnicity, medical history, and viral profile. There was a significant difference in age, with the earlier cohort being younger (median age of 1.9 mo [IQR, 1.2–3.5] vs 3.3 mo [1.7–8.6]; *p* < 0.001).

Frequency of adjunctive interventions was compared between the two time periods (**Table 2**). There was an increased use of noninvasive ventilation in the second group (94% from 69%; *p* < 0.001). The predominant modality of noninvasive ventilation in the first group was NCPAP, which was used in 66% of patients. Its use decreased significantly to 29% of patients in the later cohort (*p* < 0.001). However, as NCPAP use decreased, HFNC use increased almost 10-fold from the earlier to later cohort (89% from 9%; *p* < 0.001). There was no change in biphasic positive airway pressure use between cohorts (2% from 3%; *p* = 1.00). There was a significantly decreased usage of intubation

TABLE 1. Demographic Data of Children Who Were Admitted to the ICU and Met Study Criteria

Demographic Information	2010–2012 (<i>n</i> = 146)	2015–2016 (<i>n</i> = 179)	<i>p</i> /OR (95% CI)
Age (yr), median (25–75% IQR)	0.16 (0.10–0.29)	0.28 (0.14–0.72)	< 0.001
Male gender, <i>n</i> (%)	91 (62)	109 (61)	0.82/0.9 (0.6–1.5)
Race/ethnicity, <i>n</i> (%)			
Caucasian	65 (45)	65 (36)	0.14/0.7 (0.4–1.1)
African-American	17 (12)	24 (13)	0.74/1.2 (0.6–2.3)
Hispanic	34 (23)	47 (26)	0.61/1.2 (0.7–1.9)
Asian	7 (4)	3 (2)	0.52/1.9 (0.5–7.6)
Other	24 (16)	33 (18)	0.66/1.1 (0.6–2.0)
Medical history, <i>n</i> (%)			
Previously healthy	83 (57)	103 (58)	0.91/1.0 (0.7–1.6)
Prematurity (< 34 wk)	25 (17)	32 (18)	1.00/1.1 (0.6–1.9)
Gastroesophageal reflux disease	20 (14)	20 (11)	0.50/0.8 (0.4–1.5)
Reactive airway disease/asthma	13 (9)	25 (14)	0.22/1.7 (0.8–3.4)
Bronchopulmonary dysplasia/chronic lung disease	10 (7)	15 (8)	0.68/1.2 (0.5–2.9)
Chronic respiratory failure	6 (4)	0 (0)	0.01
Viruses, <i>n</i> (%)			
Respiratory syncytial virus	113 (77)	122 (68)	0.08
Rhino/enterovirus	0 (0)	3 (2)	0.26
Parainfluenza	1 (1)	0 (0)	0.45
Human metapneumovirus	0 (0)	1 (1)	1.00
Adenovirus	0 (0)	1 (1)	1.00

IQR = interquartile range, OR = odds ratio.

Data presented as frequency (%) or median (25–75% IQR).

and mechanical ventilation (13% from 42%; $p < 0.001$) and high-frequency oscillatory ventilation (1% from 5%; $p < 0.02$). No patients in either cohort required extracorporeal membrane oxygenation support or tracheostomy. There was also a significantly decreased rate of CVC placement (7% from 37%; $p < 0.001$) and arterial line placement (1% from 7%; $p = 0.01$). Foley catheter placement decreased from 9% to 4%, but this was not statistically significant ($p = 0.07$).

Clinical course was compared between the two time periods (Table 2). The median hospital length of stay in the later cohort was 7 days from 9.5 days in the earlier cohort ($p < 0.001$). The ICU length of stay was also significantly shorter in the latter time period (median of 3.4 vs 4.6 d; $p = 0.01$). There was no significant difference in mortality between the two groups regardless of the noninvasive treatment modality ($p = 1.00$). In the earlier cohort, all patients survived, whereas one patient succumbed to their illness in the second group.

In order to assess factors associated with CVC use, a univariate analysis was conducted (Table 3). Children who had CVC placement were significantly more likely to have a history of gastroesophageal reflux disease and chronic respiratory failure. These

children were also more likely to have received NCPAP, been intubated, have an arterial catheter placed, and have a Foley catheter placed. Of those who did not have a CVC, most were previously healthy and received support with HFNC. These patients also had shorter hospital and ICU length of stays compared with those who did not have a CVC placed.

Factors associated with CVC placement were assessed using a multiple logistic regression model constructed of the aforementioned variables associated with CVC placement on univariate analysis. The best fitting model was one that contained investigational time period, intubation, and hospital length of stay ($R^2 = 0.67$; Table 4). This suggests that these variables are all independently associated with CVC placement.

A univariate analysis was performed to evaluate factors associated with intubation finding, no association with race, gender, or chronic medical conditions. There was, however, an association between patient age and intubation, with intubated children being younger (median, 0.17 yr; IQR, 0.09–0.32 yr) compared with non-intubated children (median, 0.23 yr; IQR, 0.12–0.62 yr; $p = 0.002$). This suggests that these variables are all independently associated with CVC placement.

TABLE 2. Frequency and Duration of Interventions Compared Between the Two Time Periods

Therapies and Procedures Performed	2010–2012 (n = 146)	2015–2016 (n = 179)	p/OR (95% CI)
Died, n (%)	0 (0)	1 (1)	1.00
Therapies			
HFNC use, n (%)	13 (9)	160 (89)	< 0.001/86.1 (41.0–180.9)
HFNC days, median (25–75% IQR)	2 (1–2.5)	3 (2–4)	0.001
NCPAP use, n (%)	97 (66)	52 (29)	< 0.001/0.21 (0.13–0.33)
NCPAP days, median (25–75% IQR)	3 (2–4)	3 (2–4)	0.55
BiPAP, n (%)	4 (3)	4 (2)	1.00/0.8 (0.2–3.3)
BiPAP days, median (25–75% IQR)	1 (1–2.5)	2.5 (1.25–4.5)	0.28
Any noninvasive ventilation, n (%)	101 (69)	168 (94)	< 0.001/6.8 (3.4–13.8)
Intubation, n (%)	61 (42)	23 (13)	< 0.001/0.12 (0.12–0.36)
Intubated days, median (25–75% IQR)	10 (7.5–13)	8 (6–10.25)	0.055
High-frequency oscillatory ventilation, n (%)	7 (5)	1 (1)	0.02/0.1 (0.01–0.9)
Extracorporeal membrane oxygenation, n (%)	0 (0)	0 (0)	Not applicable
Tracheostomy, n (%)	0 (0)	0 (0)	Not applicable
Central venous catheter, n (%)	54 (37)	12 (7)	< 0.001/0.12 (0.06–0.24)
Arterial catheter, n (%)	10 (7)	2 (1)	0.01/0.2 (0.03–0.7)
Foley catheter, n (%)	13 (9)	7 (4)	0.07/0.4 (0.2–1.1)
LOS, median (25–75% IQR)			
Hospital LOS	9.5 (6–17.25)	7 (5–10)	< 0.001
ICU LOS	4.6 (2.1–10.2)	3.4 (1.6–4.9)	0.01

BiPAP = biphasic positive airway pressure, HFNC = high-flow nasal cannula oxygen, IQR = interquartile range, LOS = length of stay, NCPAP = nasal continuous positive airway pressure, OR = odds ratio.

Data presented as frequency (%) or median (25–75% IQR).

DISCUSSION

In this cohort of children with acute viral bronchiolitis, we found that respiratory failure can safely be managed with noninvasive ventilation and decreased CVC use compared with a historic control. A practice change that encouraged increased use of noninvasive ventilation was also associated with fewer CVCs, arterial catheters, and endotracheal tubes in patients. The length of stay was also significantly shortened with the increased use of noninvasive ventilation.

In 2010, McKiernan et al (20) conducted a retrospective chart review of 115 patients under 24 months with bronchiolitis who were treated with HFNC therapy at a single-center PICU. After the introduction of HFNC to their unit, they reported a 68% decrease in intubation rate in children with bronchiolitis, as well as a decrease in respiratory rate within 1 hour of initiation of HFNC therapy. Those with the largest decrease in respiratory rate were less likely to be intubated, likely reflective of the efficacy of HFNC to treat acute respiratory failure. They also found a decrease in overall PICU length of stay of the entire cohort when HFNC was used (20). Our cohort incorporated many more patients than the McKiernan et al (20) cohort and yielded very similar outcomes.

More recently, Lin et al (21) published a meta-analysis regarding the use of HFNC for children with bronchiolitis. They included nine randomized controlled trials that evaluated 2121 children with bronchiolitis and found no significant difference in hospital length of stay, length of oxygen supplementation, frequency of intubation, and adverse events in the HFNC group compared with those who received standard oxygen therapy and NCPAP (21). Although our study did not compare the difference in outcomes between noninvasive devices, nor overall hospital length of stay or total duration of oxygen supplementation, as opposed to need for PICU care, our data do support similar results that the use of HFNC is safe as a first-line modality of respiratory support and may have other benefits.

To our knowledge, this is the first study that has evaluated the association of invasive catheters and the use of noninvasive ventilation. Although invasive devices provide many benefits for the patient, they can be a nidus for bacteria and greatly increase the chance of a serious infection (11). Central line-associated bloodstream infections typically require prolonged parenteral antibiotic therapy and are tracked by both the Joint Commission and the Department of Public Health (11). CVCs and arterial catheters

TABLE 3. Univariate Analysis of Central Venous Catheter Placement

Demographic Information and Performed Therapies	CVC (<i>n</i> = 56)	No CVC (<i>n</i> = 259)	<i>p</i> /OR (95% CI)
Age (yr), median (25–75% IQR)	0.19 (0.10–0.34)	0.21 (0.12–0.61)	0.09
Male gender, <i>n</i> (%)	35 (53)	165 (64)	0.12/0.64 (0.37–1.1)
Race/ethnicity, <i>n</i> (%)			
Caucasian	24 (36)	106 (42)	0.48/0.79 (0.45–1.4)
African-American	8 (12)	13 (13)	1.00/0.12 (0.4–2.1)
Hispanic	23 (35)	58 (23)	0.06/1.8 (1.0–3.2)
Asian	3 (5)	7 (3)	0.44/1.7 (0.4–6.7)
Other	8 (12)	49 (19)	0.21/0.6 (0.3–1.3)
Medical history, <i>n</i> (%)			
Previously healthy	20 (44)	157 (61)	0.02/0.5 (0.3–0.9)
Prematurity (< 34 wk)	16 (24)	41 (16)	0.15/1.7 (0.9–3.3)
Gastroesophageal reflux disease	14 (21)	26 (10)	0.02/2.4 (1.2–4.9)
Reactive airway disease/asthma	8 (12)	30 (12)	0.83/1.0 (0.5–2.4)
Bronchopulmonary dysplasia/chronic lung disease	7 (11)	18 (7)	0.31/1.6 (0.6–4.0)
Chronic respiratory failure	4 (6)	2 (1)	0.02/8.3 (1.5–46)
Died, <i>n</i> (%)	1 (2)	0 (0)	0.20
Therapies			
HFNC use, <i>n</i> (%)	14 (21)	159 (61)	< 0.001/0.2 (0.1–0.3)
Days on HFNC, <i>n</i> (%)	2 (2–4)	3 (2–4)	0.01
NCPAP use, <i>n</i> (%)	40 (61)	109 (42)	0.01/2.1 (1.2–3.7)
Days NCPAP, median (25–75% IQR)	2 (1–4.25)	3 (2–4)	0.15
BiPAP, <i>n</i> (%)	3 (5)	5 (2)	0.21/2.4 (0.6–10.4)
Days BiPAP, median (25–75% IQR)	1 (1–5)	2 (1–3)	0.87
Any noninvasive ventilation use, <i>n</i> (%)	47 (71)	222 (86)	0.01/0.4 (0.2–0.8)
Intubation, <i>n</i> (%)	62 (94)	22 (8)	< 0.001/167 (56–502)
Days of intubation, median (25–75% IQR)	10 (8–13)	8 (6–9.5)	0.01
High-frequency oscillatory ventilation, <i>n</i> (%)	7 (11)	1 (0)	< 0.001/31 (4–254)
Extracorporeal membrane oxygenation, <i>n</i> (%)	0 (0)	0 (0)	Not applicable
Tracheostomy, <i>n</i> (%)	0 (0)	0 (0)	Not applicable
Arterial catheter, <i>n</i> (%)	10 (15)	2 (1)	< 0.001/23 (5–108)
Foley catheter, <i>n</i> (%)	17 (26)	3 (1)	< 0.001/30 (8–105)
Length of stay			
Hospital (d), median (25–75% IQR)	18 (14–26)	7 (5–9)	0.001
ICU (d), median (25–75% IQR)	10.8 (8.2–15.1)	3.1 (2.1–4.5)	< 0.001
Time period, <i>n</i> (%)	54 (82)	12 (18)	< 0.001/0.1 (0.1–0.2)

BiPAP = biphasic positive airway pressure, CVC = central venous catheter, HFNC = high-flow nasal cannula oxygen, IQR = interquartile range, NCPAP = nasal continuous positive airway pressure, OR = odds ratio.

Data presented as frequency (%) or median (25–75% IQR).

TABLE 4. Multiple Logistic Regression Model of Factors Associated With Central Venous Catheter Placement

Variable	Coefficient (β)	SE	Wald χ^2	p	OR (95% CI)
Intercept	2.86	0.55	0	< 0.001	—
Hospital Length of Stay	-0.06	0.02	8.9	0.003	0.94 (0.90–0.98)
Intubation	2.50	0.35	52.0	< 0.001	148.6 (45.0–749.3)
Time Period	-0.80	0.26	9.4	0.002	5.0 (1.8–14.2)

also carry significant thrombotic risks that could have prolonged consequences even postdischarge (22), as well as carry the risk of death. Therefore, avoidance of using these devices can potentially help limit complications of acute illness.

Prolonged ICU stays are associated with patient physical, psychologic, cognitive, and functional deconditioning, decreased perceived quality of life, and social hardships for the patient and their family (22, 23). De-intensifying patients, by using less-invasive devices, may promote earlier discharge from both the ICU and the hospital. Additionally, an increased number of invasive procedures performed is known to be a hindrance to patient mobility and is a risk factor for development of ICU-related morbidities (23). Others have reported that early rehabilitation may improve outcomes and shorten ICU length of stay (24, 25). It may be that limiting invasive procedures may significantly decrease both the short- and long-term complications in critically ill patients, as well as shorten their length of stay.

This study has several limitations. All subjects were identified from a single center, and thus, our data may not be generalizable to the entirety of patients in this age group with viral bronchiolitis. Additionally, no explicit guidelines regarding the rationale of when to implement each method of respiratory support are present, and therefore, there may be cognitive bias due to variability of individual provider preference and medical decision-making. Our cohorts were matched by chronology of admission rather than severity of illness, but our large sample size, and well-matched study groups, should account for variability in illness severity. The only statistically significant demographic difference between the two groups analyzed was regarding age, with the earlier cohort being younger. Younger children are at risk for a more severe illness course, which could contribute to the increased rate of intubations in this cohort.

CONCLUSIONS

Our data support that a practice change toward managing patients with acute respiratory failure secondary to bronchiolitis with less-invasive means is possible without compromising patient outcome. The use of HFNC was associated with a reduction in the use of other invasive devices, specifically endotracheal tubes, CVCs, arterial catheters, and there was a significantly decreased hospital length of stay following the implementation of a practice change toward increased noninvasive devices. Additionally, it may be that minimizing the use of invasive ventilation and thereby reducing the use of other invasive devices could potentially have additional benefits such as reduced hospital-acquired complications.

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