Original Article

Risk factors for intubation among less than 2-year-old patients with bronchiolitis admitted to pediatric intensive care unit (PICU) that implements early high flow nasal cannula: a retrospective cohort study

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Background: Severe bronchiolitis within seasonal outbreaks is increasing. This places significant strain on pediatric intensive care unit (PICU) resources and capacity. Non-invasive ventilation (NIV) and high flow nasal cannula (HFNC) have reduced rates of intubation and conventional mechanical ventilation (CMV) but risk factors and mitigation strategies continue to be elucidated. The primary objective of this study was to identify bronchiolitis intubation risk factors within a provincial protocol for HFNC. Secondarily intubation rates before and after implementation of the protocol were evaluated.

Methods: A retrospective chart review was conducted on all <2-year patients with bronchiolitis admitted every year to Saskatchewan's PICU from November to March between 2015 and 2023. Risk factors for bronchiolitis intubation within a provincial HFNC protocol were evaluated. The primary outcome was variables associated with intubation. Bivariate analyses compared descriptive and admission variables between the intubated and non-intubated cohorts. Analyses were completed on STATA 14 software.

Results: One hundred and eighty-two patients met criteria, and 19 (10.4%) required intubation. Risk factors for intubation were multiple viruses (P=0.02), secondary bacterial infection (P<0.001) and elevated C-reactive protein (CRP) (P=0.003). Intubated patients had longer PICU length of stay (8.16 *vs.* 4.16 days; P<0.001). There was a statistically significant (27 of 148 *vs.* 19 of 182; P=0.04) decrease in intubation rates following provincial HFNC protocol initiation.

Conclusions: A protocol driven provincial HFNC algorithm for early respiratory support may promote decreased intubation rates in severe bronchiolitis. Within the same structure risk factors such as multiple viruses, concomitant infections and elevated CRP may serve as early warning for bronchiolitis patients at higher risk for intubation.

Keywords: Bronchiolitis; high flow nasal cannula (HFNC); pediatrics; mechanical ventilation; non-invasive ventilation (NIV)

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Introduction

Background

Severe bronchiolitis is an important cause of pediatric intensive care unit (PICU) admissions. Seasonal outbreaks of pathogens that cause bronchiolitis, like respiratory syncytial virus (RSV), place enormous pressures on PICU resources and capacity (1). However, despite public health initiatives utilizing RSV preventative antibody products, PICU admissions continue to rise in high income countries (1-3).

For the past quarter century, ventilatory protocols utilizing high flow nasal cannula (HFNC), and non-invasive ventilation (NIV) including continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP) have been developed. HFNC may be related to reduced intubation rates (3-5). Observational studies suggest an inverse correlation between NIV support and need for subsequent conventional mechanical ventilation (CMV) (4,6,7). A recent systematic review and meta-analysis concluded from five randomized controlled trials that CPAP was associated with lower risk of treatment failure but higher adverse events than HFNC (8).

Highlight box

Key findings

- A provincial algorithm for early high flow nasal cannula (HFNC) and noninvasive ventilation (NIV) support may promote decreased intubation rates in severe bronchiolitis.

What is known and what is new?

- The need for conventional mechanical ventilation (CMV) in children with bronchiolitis can strain resources and capacity for pediatric intensive care units. It also introduces young children to the necessities of CMV including central acting medications and nasogastric feeds, and increased risks of ventilator associated pneumonias.
- Risk factors for intubation were multiple viruses (P=0.02), secondary bacterial infection (P<0.001) and elevated C-reactive protein (P=0.003). There was a statistically significant (27 of 148 *vs.* 19 of 182; P=0.04) decrease in intubation rates following provincial HFNC protocol initiation.
- The use of HFNC and NIV in children with bronchiolitis has reduced the requirements for CMV. However, the effects of improving earlier access to respiratory support have not been reported.

What is the implication, and what should change now?

- Healthcare jurisdictions can consider ways to optimize early respiratory support by creating algorithms for HFNC support on the wards and NIV with interfacility transport teams.

Rationale and knowledge gap

Despite the availability of HFNC and NIV, CMV may be necessary in 10–15% of RSV bronchiolitis (9,10) and 25% for non-RSV bronchiolitis admitted to the PICU (10). A single-site study of 573 patients reported intubation risk factors for critically ill patients with bronchiolitis as younger age, history of prematurity, neurologic or genetic co-morbidities and presence of multiple positive pathogens (11). Age less than 6 months (3,12), prematurity (3,13), lower hemoglobin (14), major chronic conditions (3) and interhospital transport (3) have been reported elsewhere. These studies, however, did not evaluate the timing of HFNC and/or NIV initiation regarding intubation risk factors, and may suggest modifiable clinical practices to decrease the need for CMV.

Objective

The primary purpose of this retrospective study was to study risk factors for intubation in bronchiolitis patients within a provincial protocol that implements early HFNC in regional health centers. Secondarily, intubation rates before implementation of the provincial HFNC were compared to current rates of intubation. We present this article in accordance with the STROBE reporting checklist (available at https://pm.amegroups.com/article/view/10.21037/pm-23-78/rc).

Methods

This retrospective cohort study evaluated all pediatric patients admitted to a tertiary PICU every year from November to March between 2015 and 2023 with a diagnosis of bronchiolitis. The first 3 years included data before the provincial HFNC protocol was implemented. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the University of Saskatchewan Health Ethics Board (No. #3280) and individual consent for this retrospective analysis was waived due to the retrospective nature of the study together with the high number of charts reviewed.

Subjects

Search criteria in a PICU database identified all pediatric patients (<2 years of age) admitted with bronchiolitis. This included all patients who failed HFNC on the wards

according to a provincial algorithm (15) and/or required >0.50 FiO_2 on HFNC, NIV or CMV. Patients excluded from the study had either advanced care directives, known cardiac pathophysiology or neuromuscular disease.

Upon admission to hospital, all patients received a nasal pharyngeal swab which was analysed via in-lab polymerase chain reaction for RSV, adenovirus, influenza A/B, coronaviruses, parainfluenza virus types 1–4, human metapneumovirus, and rhinovirus. An admission to the PICU resulted in a complete blood count with differential, extended electrolytes, venous blood gas and a C-reactive protein (CRP). If patients were febrile and had an elevated white blood cell count and/or a CRP >50 mg/dL, blood, urine and endotracheal cultures (when applicable) were obtained.

Saskatchewan context

A provincial algorithm for general pediatric ward patients with bronchiolitis requiring HFNC was developed for regional health centers (15). These patients are managed in pediatric units capable of continuous cardiorespiratory monitoring, and frequent respiratory interventions and evaluations through increased nurse and/or respiratory therapy support. After 90 minutes of HFNC, non-responders are defined by a FiO_2 >0.50, increase in Pediatric Early Warning System (PEWS) respiratory score, or red PEWS score (PEWS score 3 in any category).

Non-responders to the provincial HFNC algorithm are transferred to a single tertiary PICU by its specialized pediatric transport team. Depending on the patient's work of breathing, respiratory rate, FiO_2 requirements, and other variables, NIV or intubations leading to CMV can be initiated early by the pediatric transport team (16) or in the PICU.

Criteria for intubation

The decision to intubate bronchiolitis patients is made by the on service pediatric intensivist. The criteria generally include: high FiO_2 requirements with recurrent desaturations; apneas with bradycardia; significant decreases in minute ventilation; and worsening respiratory acidemia. Prior to consideration of intubation non-invasive respiratory support is escalated to CPAP and then BiPAP. Maximal BiPAP settings generally include inspiratory positive airway pressures of 18 cm H_2O, expiratory positive airway pressures 12 cmH_2O and backup rate of 20 at the lowest sensitive flow-trigger.

Statistical analysis

All data was obtained from electronic health records. Descriptive data included age at presenting hospital, sex, day of illness, comorbidities and premature birth. Admission data included need for interfacility transport, RSV positive, multiple viruses, secondary bacterial infection, hemoglobin, white blood cell count, and CRP. Outcomes included need for CMV, PICU length of stay and mortality.

The primary outcome was variables associated with intubation. Bivariate analyses compared descriptive and admission variables between the intubated and non-intubated cohorts. Proportions were compared using the chi-squared test. Mean, standard deviations and difference of means were calculated for continuous variables. Intubation rates prior to the implementation of a provincial protocol were also compared to intubation rates thereafter using the chi-squared test. All statistics for P values were two-tailed. Statistical significance was considered using an alpha of 0.05. Analyses were completed on STATA 14 software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX, USA: StataCorp LP).

Results

One hundred and eighty-three patients were identified from our PICU registry that met our inclusion criteria. All but one electronic chart was available and/or complete for review and were included in the study. Patient characteristics and admission data are summarized in *Table 1*. Of the 182 patients evaluated, 19 (10.4%) required intubation. Nine of the intubations (47%) were done in referring centers, two (11%) in the tertiary center's emergency department and 8 (42%) in the PICU. Risk factors for intubation included multiple viruses (P=0.02), secondary bacterial infection (P<0.001) and elevated CRP (P=0.003). Intubated patients also had a significantly longer PICU length of stay (8.16 *vs.* 4.16 days; P<0.001). There were no mortalities. Finally, our rates of intubation (27 of 148; 18.2%) prior to the implementation of a provincial HFNC algorithm were significantly higher (P=0.04).

Discussion

Key findings

To our knowledge, this is the first study to examine intubation risks for severe bronchiolitis by optimizing early respiratory support outside the PICU. Utilizing a provincial

Table 1 Risk factors for intubation

Variables	Total (n=182)	Intubated (n=19)	Non-intubated (n=163)	P value[†]
Age (days), mean [SD]	169 [144]	157 [159]	171 [141]	0.70
Sex (male), n (%)	100 (54.9)	8 (42.1)	92 (56.4)	0.25
Premature birth, n (%)	34 (18.7)	5 (26.3)	29 (17.8)	0.37
Comorbidities, n (%)	48 (26.4)	4 (21.1)	44 (27.0)	0.58
Day of presentation (days), mean [SD]	–	3.47 [1.76]	3.73 [1.74]	0.58
RSV positive, n (%)	126 (69.2)	11 (57.9)	115 (70.6)	0.26
Multiple viruses, n (%)	61 (33.5)	11 (57.9)	50 (30.7)	0.02
Secondary bacterial infection, n (%)	9 (4.9)	5 (26.3)	4 (2.5)	<0.001
White blood cell count ($\times 10^9$/L), mean [SD]	10.77 [4.71]	11.26 [6.08]	10.75 [4.48]	0.66
Hemoglobin (g/L), mean [SD]	114.7 [17.3]	110.7 [20.7]	115.2 [16.7]	0.28
C-reactive protein (mg/L), mean [SD]	36.8 [48.2]	70.4 [61.8]	32.5 [44.2]	0.003

[†], P value of intubated versus non-intubated patients. SD, standard deviation; RSV, respiratory syncytial virus.

HFNC protocol in regional referring centers and a tertiary hospital, the risk factors for intubation included multiple viruses, concomitant bacterial infections, and an elevated CRP.

Strengths and limitations

Our HFNC protocol for regional health centers helped to assure timely and standardized care throughout the province. By providing early respiratory support to patients that may be presented to regional hospitals hundreds of kilometers from our PICU, system factors that could have contributed to early intubation were mitigated. There are, however, a few limitations to our study. First, it was a single center retrospective study that may not be generalizable to centers without a coordinated protocol in referring centers or a specialized pediatric transport team. Second, the decision to intubate patients with bronchiolitis is at the discretion of the pediatric intensivist. Hence, our primary outcome was not part of protocolized care.

Comparison with similar research

The presence of multiple positive pathogens has been previously reported (11), but the time lag for positive results restricts their clinical usefulness particularly during the triage phase. Despite previous studies suggesting otherwise (3,9-14), we did not find young age, prematurity, comorbidities, anemia, non-RSV bronchiolitis and interfacility transport as risk factors for intubation.

Explanation of findings

While it is somewhat intuitive for these risk factors to be stated in the context of inflammation in small airways, we believe that our provincial protocol for early access to HFNC and NIV has mitigated many of those previously described. In support, we have seen a significant decrease to our historical intubation rates as the protocol has been implemented.

We expected prematurity, young age, and even the presence of comorbidities to increase the risk of intubation. Their susceptible lung parenchyma and/or smaller airways should have led to greater hypoxemia, atelectasis and ventilation/perfusion mismatching. However, the most responsible aspect of our protocol to account for this negative finding is unknown. The protocol has empowered regional centers to initiate HFNC early and to promptly identify patients who need to escalate support to NIV. In many instances, this would have resulted in a timely consultation with a pediatric intensivist who would have organized an interfacility transportation to the PICU.

Implications and actions needed

CRP may have the potential to promptly determine intubation risks in severe bronchiolitis. A larger cohort may be necessary to elucidate threshold values, but our study

found a mean CRP more than twice as high in the intubated group (70.4 *vs.* 32.5 mg/L). Dissimilar to pathogen testing, this lab value can be promptly processed, and at the very least, present a red flag to practitioners for more diligent monitoring.

Early access to increased respiratory support is a healthcare system challenge, particularly for large health regions. Many smaller or regional centers can escalate support in adults, but often lack the expertise and/or supplies to manage children at the younger ages. The creation of pediatric clinical pathways and triage algorithms with tertiary centers is often the standard, but solutions should be sought to safely escalate respiratory whenever required.

Conclusions

In summary, compared to previously reported, our study rendered specific risk factors and lower rates of intubation for patients with bronchiolitis treated within the setting of a protocol driven provincial HFNC algorithm. We found multiple viruses, concomitant infections and elevated CRP were related to risk of intubation. Future studies evaluating CRP thresholds may further allow prediction of bronchiolitis intubation risk.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://pm.amegroups.com/article/view/10.21037/pm-23-78/rc

Data Sharing Statement: Available at https://pm.amegroups.com/article/view/10.21037/pm-23-78/dss

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Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://pm.amegroups.com/article/view/10.21037/pm-23-78/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the University of Saskatchewan Health Ethics Board (No. #3280) and individual consent for this retrospective analysis was waived due to the retrospective nature of the study together with the high number of charts reviewed.

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