Respiratory Modalities in Preventing Reintubation in a Pediatric Intensive Care Unit

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Abstract
Post-extubation respiratory failure requiring reintubation in a Pediatric Intensive Care Unit (PICU) results in significant morbidity. Data in the pediatric population comparing various therapeutic respiratory modalities for avoiding reintubation is lacking. Our objective was to compare therapeutic respiratory modalities following extubation from mechanical ventilation. About 491 children admitted to a single-center PICU requiring mechanical ventilation from January 2010 through December 2017 were retrospectively reviewed. Therapeutic respiratory support assisted in avoiding reintubation in the majority of patients initially extubated to room air or nasal cannula with high-flow nasal cannula (80%) or noninvasive positive pressure ventilation (100%). Patients requiring therapeutic respiratory support had longer PICU LOS (10.92 vs 6.91 days, P-value = .0357) and hospital LOS (16.43 vs 10.20 days, P-value = .0250). Therapeutic respiratory support following extubation can assist in avoiding reintubation. Those who required therapeutic respiratory support experienced a significantly longer PICU and hospital LOS. Further prospective clinical trials are warranted.

Keywords
critical care, airway extubation, respiratory failure, high-flow nasal cannula, reintubation

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Introduction
Reintubation occurs in approximately 10% to 23% of elective extubations.1-3 The need for reintubation is associated with an increased risk of complications such as ventilator-associated pneumonia, prolonged intensive care unit (ICU), and hospital length of stay (LOS), increased likelihood to require transfer to a long-term care facility, and an increased risk of mortality.1,3,4 The majority of the data is derived from studies in the adult population. While studies of extubation failure in specific pediatric populations have been investigated, sparse information is available on patients in the pediatric ICU (PICU).5-11 Ensuring patient readiness and optimizing post-extubation respiratory support are critical interventions to help avoid the need for reintubation. Immediately after elective extubation, patients are frequently supported with supplemental oxygen. These oxygen delivery modalities include support with oxygen via blow-by or aerosol mask, nasal cannula, high-flow nasal cannula (HFNC), and noninvasive positive pressure ventilation (NIPPV), which comprises CPAP and BiPAP. Patients with post-extubation respiratory distress require enhanced oxygen delivery with a therapeutic respiratory modality in an attempt to prevent reintubation. The main objective of this study was to evaluate the success of different therapeutic respiratory modalities in avoiding reintubation in patients experiencing post-extubation respiratory distress.

Materials and Methods
A retrospective review of pediatric patients (<18 years old) admitted to a single-center PICU who required...
mechanical ventilation from January 2010 to December 2017 was performed. Exclusion criteria included: patients with a tracheostomy, history of home oxygen support, patients who underwent recent airway reconstructive surgery, patients who were intubated with admission to another ICU before transfer to our institution, or patients that had unplanned extubation. Data were collected on patient demographics, diagnosis at presentation, the reason for intubation, length of intubation, oxygen delivery modality used following extubation, pre- and post-extubation blood gas values, the need for reintubation, PICU LOS, and hospital LOS.

Therapeutic respiratory modalities were administered via 1 of 4 ways: nasal cannula (for patients extubated to room air, blow-by, or aerosol mask), HFNC (for patients extubated to nasal cannula, room air, blow-by, or aerosol mask), and NIPPV or non-rebreather (for patients extubated to HFNC, nasal cannula, room air, blow-by, or aerosol mask) (Table 1). Extubation failure was defined as post-extubation respiratory distress requiring reintubation within 48 hours of elective extubation.

The Pediatric Index of Mortality 2 (PIM2) score, which estimates the mortality risk in the pediatric population, was used to compare the severity of illness between cohorts. Continuously measured variables are reported with the mean and median with standard deviations and interquartile ranges (IQR), respectively. Categorical variables are reported as frequencies with percentages. Differences between the various cohorts were analyzed with 2 Samples Independent T-Tests and Chi-square tests for continuous and categorical variables, respectively. All analyses were done in SAS 9.4 (SAS Institute Inc., Cary, NC, USA) with a P-value < .05 indicating statistical significance.

Ethical Approval and Informed Consent
This study was approved by the Beaumont Health Institutional Review Board (#2018-135). The need to obtain consent for the collection, analysis, and publication of the retrospectively obtained and anonymized data for this non-interventional study was waived.

Table 1. Therapeutic Respiratory Modality Options.

| Initial oxygen support                      | Therapeutic respiratory modality options       |
|--------------------------------------------|-----------------------------------------------|
| Room air, aerosol mask, blow-by            | Nasal cannula, HFNC, NIPPV, non-rebreather     |
| Nasal cannula                              | HFNC, NIPPV, non-rebreather                    |
| High-flow nasal cannula                    | NIPPV, non-rebreather                          |

Abbreviations: HFNC, high-flow nasal cannula; NIPPV, noninvasive positive pressure ventilation.

Table 2. Demographics.

|                |                   |                  |
|----------------|-------------------|------------------|
| Gender         | Male              | 283 (57.64%)     |
|                | Female            | 208 (42.36%)     |
| Age at admission (years, IQR) | 5.00 (0.00-14.00) |
| Length of intubation (hours, IQR)   | 19.25 (6.50-55.50) |
| PICU length of stay (days, mean with SD) | 7.21 ± 9.21 |
| Hospital length of stay (days, mean with SD) | 10.67 ± 12.02 |

Abbreviations: IQR, interquartile range; PICU, pediatric intensive care unit; SD, standard deviation.

Results
About 491 patients met our inclusion criteria over the 8-year retrospective review. The median age was 5.00 years (IQR 0.00-14.00) (Table 2). The most common indications for initial intubation were respiratory failure (34.5%) (ie, upper respiratory tract infection, pneumonia, status asthmaticus, airway obstruction, and anaphylaxis), need for surgery or procedure (34.3%) (ie, elective or emergent surgery, sedation for an invasive procedure or imaging), and altered mental status (31.5%) (ie, chemical or drug intoxication, status epilepticus, and trauma). The median length of intubation for the cohort was 19.25 hours (IQR 6.50-55.50 hours). PIM2 and Risk of Mortality (ROM) scores were similar across all treatment groups with no significant difference, indicating similar severity of illness. The initial modalities used for supplemental oxygen delivery post-extubation included 58 patients (11.81%) extubated to room air, blow-by, or aerosol mask, 337 patients (68.64%) extubated to HFNC, 75 patients (15.27%) extubated to nasal cannula, room air, blow-by, or aerosol mask (Table 3). There was a significant difference in the average age of patients extubated to room air, blow-by, or aerosol mask (9.32 years ± 6.55) and nasal cannula (7.37 years ± 6.36) compared to patients extubated to HFNC (4.31 years ± 5.93) (P-value < .0001 and .0002, respectively). Unlike HFNC, patients extubated to NIPPV were not significantly younger (6.73 years ± 6.99) (P-value = .1161). Additionally, the average PICU LOS was significantly shorter for patients extubated to room air, blow-by, or aerosol mask (3.23 days ± 4.22) and
nearly on clinical judgment faired quite successfully. About 89.41% of the patients were extubated without issue or need for escalating care. About 7.74%

Discussion

The decision to extubate a patient receiving mechanical ventilation requires a full assessment of the patient’s readiness to breathe on their own. Respiratory failure post-extubation requiring reintubation may result in significant consequences, including an increased risk of complications (ie, ventilator-associated pneumonia), prolonged ICU and hospital LOS, increased likelihood to require transfer to a long-term care facility, and an increased risk of mortality.\(^1,3,4\) Evaluating efforts to reduce the incidence of reintubation is critical and can be accomplished by improving pre-extubation assessment and optimizing post-extubation therapeutic respiratory modalities. Contrary to the adult literature, where indices like negative inspiratory pressure and rapid shallow breathing index have proven to be reliable markers in predicting extubation success, a systematic review of mechanically ventilated pediatric patients failed to suggest any validated method of assessing readiness or predicting successful extubation superior to clinical judgment in the pediatric population.\(^12\) They cited an extubation failure rate of 2%-20% and notably found no relationship between the duration of mechanical ventilation and the need for reintubation, both of which were supported by our study.\(^12\) Even with the use of modern tools and assessments, adult ICUs still experience a reintubation rate of 10%-20% following elective extubations.\(^1,3,4\) In our cohort, no specific markers or indices were consistently used to determine the readiness for extubation, but rather all patients were put through a spontaneous breathing trial and evaluation by the PICU team with the ultimate decision for extubation being made based upon the clinical judgment of the rounding pediatric intensivist.

When evaluating our outcomes, extubating primarily on clinical judgment faired quite successfully. About 89.41% of the patients were extubated without issue or need for escalating care. About 7.74%
required a therapeutic respiratory modality, which appears to have assisted in avoiding reintubation in 84.21% of patients, and only 2.85% proceeded directly to reintubation without the use of any therapeutic respiratory modality. Further analysis revealed that patients extubated to less intense modes of oxygen delivery had statistically significant shorter PICU and hospital LOS compared to patients extubated with more intensive methods of delivery, suggesting that providers were accurately predicting the patients with a more challenging course and requiring more intensive respiratory support. Additionally, we found that patients extubated to HFNC were significantly younger than patients extubated to room air or nasal cannula, indicating that our providers were more cautious in the extubation of younger patients.

Patients who developed signs of respiratory failure (inability to maintain adequate blood oxygen saturation, labored breathing, and altered mental status) and did not require immediate reintubation were initiated on a

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**Table 4.** Potential Risk Factors for Requiring Therapeutic Respiratory Support.

| Risk factors                        | Therapeutic respiratory support | No therapeutic respiratory support | P-value |
|-------------------------------------|---------------------------------|-----------------------------------|---------|
| Gender                              | 17F/19M                         | 192F/263M                        | .6357   |
| Age at admission (years, mean with SD) | 8.84 ± 6.54                     | 6.96 ± 6.45                      | .0885   |
| Length of intubation (hours, mean with SD) | 84.5 ± 111.18                  | 65.85 ± 416.38                   | .4864   |
| Pre-extubation labs                 | (Table 5)                       | (Table 5)                        | All > .05 |

**Table 5.** Comparison of Pre-Extubation Lab Values for Patients Requiring Therapeutic Respiratory Support.

| Pre-extubation labs                                       | Therapeutic respiratory support | No therapeutic respiratory support | P-value |
|----------------------------------------------------------|---------------------------------|-----------------------------------|---------|
| pH (mean with SD)                                         | 7.40 ± 0.06                     | 7.40 ± 0.05                       | .6954   |
| SaO2 (%) (mean with SD)                                  | 98.84 ± 1.80                    | 98.62 ± 5.86                      | .5983   |
| FiO2 (%) (mean with SD)                                  | 38.92 ± 12.97                   | 39.88 ± 15.40                     | .7124   |
| pCO2 (mmHg, mean with SD)                                | 40.03 ± 6.36                    | 40.81 ± 6.58                      | .5137   |
| Bicarbonate (mmol/L, mean with SD)                       | 24.41 ± 4.16                    | 24.75 ± 3.75                      | .6269   |

Abbreviations: SaO2, oxygen saturation; FiO2, fraction of inspired oxygen; pCO2, partial pressure of carbon dioxide; SD, standard deviation; mmHg, millimeters of mercury; mmol/L, millimoles per liter.

**Table 6.** Comparison of PICU and Hospital LOS for Patients Requiring Therapeutic Respiratory Support.

|                             | Therapeutic respiratory support | No therapeutic respiratory support | P-value |
|-----------------------------|---------------------------------|-----------------------------------|---------|
| PICU LOS (days, mean with SD) | 10.92 ± 10.92                   | 6.91 ± 9.00                       | .0357   |
| Hospital LOS (days, mean with SD) | 16.43 ± 15.92                  | 10.20 ± 11.55                     | .0250   |

Abbreviations: PICU, pediatric intensive care unit; LOS, length of stay; SD, standard deviation.

**Table 7.** Success of Therapeutic Respiratory Modalities Used in the Study.

| Therapeutic respiratory modality | Initial oxygen support | Success |
|----------------------------------|------------------------|---------|
| Nasal cannula                    | Room air, blow by, aerosol mask | 2 of 2 (100%) |
| High-flow nasal cannula          | Room air, blow by, aerosol mask, or nasal cannula | 12 of 15 (80%)* |
| Noninvasive positive pressure ventilation | Room air, blow by, aerosol mask, or nasal cannula | 8 of 8 (100%)* |
|                                  | High-flow nasal cannula | 2 of 3 (66%) |
| Non-rebreather                   | Nasal cannula           | 6 of 8 (75%) |
|                                  | High-flow nasal cannula | 2 of 2 (100%) |

*No significant difference, P-value = .5257.
therapeutic respiratory modality to increase oxygen delivery in an attempt to avoid reintubation. Multiple factors were explored as potential risk factors for requiring therapeutic respiratory support. Patient gender, age at admission, the reason for intubation, length of intubation, pre-extubation lab values, and oxygen support did not result in any significance in whether a patient would require therapeutic respiratory support. While this list is likely not exhaustive, it likely does represent mostly commonly described factors. The most common therapeutic respiratory modality used in our cohort was HFNC (39.47%), followed by NIPPV (28.95%), non-rebreather (26.32%), and nasal cannula (5.26%).

Traditionally, NIPPV with CPAP or BiPAP has effectively been used as the primary therapeutic respiratory modality. However, HFNC is increasingly prevalent as it provides several potential benefits as it delivers humidified, heated air at high flow, purportedly reducing anatomic dead space, maintains pharyngeal airway pressures, reduces airway resistance, and increases mucus clearance, thereby improving ventilation and oxygenation. Furthermore, HFNC is reported to be more comfortable, tolerable, with a lower incidence of nasal trauma (when compared to nasal CPAP) than NIPPV. With HFNC being an appealing option, several studies have been conducted to compare outcomes to NIPPV. Studies focusing on infants (premature and term) and adults failed to demonstrate any significant superiority of 1 mode of therapy over the other in avoiding reintubation. However, no previous comparison was found evaluating specifically patients in the PICU, hence the impetus for our study. Our findings were similar to the findings in other cohorts; both HFNC and NIPPV appeared to successfully rescue the majority of patients from requiring reintubation (80.00% and 100%, respectively) without demonstrating any significant superiority of 1 modality over the other (P-value = .5257). Further prospective studies are warranted in this realm to clarify and determine if any significant difference exists between HFNC and NIPPV.

This study is not without limitations. It is a single-center, retrospective study; therefore, it is subject to potential bias that may have influenced our practices and outcomes. Our sample size was not sufficient enough to achieve statistical significance regarding superiority of HFNC versus NIPPV, and we acknowledge that a larger sample size could incur more precision and possibly delineate the presence of any significant difference in outcomes between therapeutic respiratory modalities. Although limited data is available with regards to therapeutic respiratory modalities in the PICU, comparable studies evaluating therapeutic respiratory modalities in other cohorts reached similar conclusions. Another limitation was our ability to risk adjust for our patient population adequately. PIM2 ROM admission mortality scores were calculated using the available data. To our knowledge, there is no validated pediatric mortality risk methodology score at 1 exact point in time more than 4 hours after admission. Thus, we cautiously chose to use these scores to risk evaluate our patients as best as possible to provide some risk-adjusted patient data.

Conclusion

Our review further suggests that clinical judgment for determining readiness for extubation appears reasonably accurate and reliable. Additional investigation of other indices to improve accuracy is still needed to approach the goal of reducing or eliminating the need for reintubation. Therapeutic respiratory support, including noninvasive positive pressure ventilation and high-flow nasal cannula, appears to help reduce the need for reintubation in the majority of patients experiencing post-extubation respiratory failure. However, further randomized prospective clinical trials may add to the findings of this paper and help to establish the causality of the associations found in this study.

Author Contributions

AA, ML, BA, PK contributed to the concept and design. AA and ML contributed to the data acquisition. AA, ML, PK, BA, PK contributed to the data analysis, data interpretation, and critical revision of the content.

Declaration of Conflicting Interests

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