Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 03/18/2021
Approved on: 09/02/2021

ORIGINAL ARTICLE

Risk factors associated with extubation in a pediatric intensive care unit

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Keywords:
Pediatrics,
Risk Factors,
Extubation,
Ventilation,
Child,
Adolescent.

Abstract

Mechanical ventilation is the ventilatory support used to support lung function while the cause of intubation is reversed. It has greatly contributed to the survival increase in intensive care units. However, the need for endotracheal intubation, especially for prolonged periods, has brought concerns about the inability of patients to sustain breathing after the removal of mechanical ventilation. Extubation failure is a worldwide problem, and the search for predictors, risk factors, and therapies to prevent it from occurring has mobilized numerous research groups. We present the results of an observational study performed in a pediatric intensive care unit for a year, which aimed to identify the risk factors related to extubation failure in children and adolescents on mechanical ventilation for at least 48 hours. We included 85 children aged between 29 days and 15 years, of which 11 (12.9%) required reintubation. The risk factors identified in our population were age of less than three months [OR: 2.71], spending more than 15 days on mechanical ventilation [OR: 7.30], shock [OR: 2.45], cardiac arrest [OR: 8.0], and replacement of endotracheal tube [1.97]. These conditions increased the risk of extubation failure in our population.

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DOI: 10.25060/residpediatr-2022.v12n4-591

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INTRODUCTION

Mechanical ventilation has greatly contributed to increased survival in pediatric and neonatal intensive care units. About 40% of the children admitted to intensive care units are intubated and placed on mechanical ventilation and up to 20% of them will experience extubation failure and consequent increases in the length of hospital stay and risk of complications and death[1-6].

Extubation failure is defined as the need to reinsert the endotracheal tube to resume mechanical ventilation in patients extubated for less than 48 hours[6,7]. In most cases, failure is due to laryngeal edema, muscle failure, cardiovascular dysfunction, acid-base disorders, or residual lung disease[8-10].

Many authors have sought to establish the predictors of extubation failure, its risk factors and therapies to prevent it from occurring. Results vary, given the heterogeneity of patients in terms of age, causes for intubation, number of attempts, tube size, ventilation parameters and mode, hemodynamic and nutritional status, and arterial blood gas levels[1,2,7,10-12].

This study aimed to identify the possible risk factors related to extubation failure in children and adolescents aged 29 days to 15 years on mechanical ventilation for more than 48 hours.

METHODS

This observational study was performed at the Pediatric Intensive Care Unit (PICU) of the Teaching Hospital of the School of Medicine of Botucatu / São Paulo State University between September 1, 2017 and August 31, 2018. It included patients aged 28 days to 15 years on mechanical ventilation for 48 hours or longer. The Research Ethics Committee of the institution approved the study (certificate no. 2.339.445).

Individuals with a tracheostomy, upper airway anomalies, laryngomalacia, neuromuscular diseases, accidental extubation without need for reintubation, and on prior treatment with steroids or immunosuppressants were excluded from the study.

Once the patients' parents/guardians signed the informed consent form, they were asked to answer a questionnaire designed to capture the following information:

- Demographic profile (age, sex, ethnicity, and body weight);
- Suspected diagnosis at admission;
- PRISM (Pediatric Risk Index Score for Mortality) score;
- Causes of intubation;
- Complications during PICU stay;
- Results of daily arterial blood gas tests;
- Daily ventilation parameters;

The patients were connected to Hamilton (HAMILTON MEDICAL AG - SWITZERLAND) Raphael Color, Galileu Gold or G5 ventilators on pressure-regulated, volume control, or pressure-regulated volume control (PRVC) mode depending on PICU procedures. Patients were assessed daily based on the Comfort scale for sedation and pain management. The position of the endotracheal tube on the corner of the mouth was checked and pressure was measured in patients equipped with tubes with a pilot balloon. Once extubation was scheduled, the patients were ventilated on pressure support (PS) mode and submitted to spontaneous breathing trials. Patients passing the trial and presenting satisfactory resolution of the condition that required ventilatory support, without increases in ventilatory parameters or FiO_2 greater than 0.5 in the last 24 hours, who reached an acceptable level of consciousness without acid-base disorders, and who would not require sedation or intubation for short-term procedures, were considered candidates for extubation.

STATISTICAL ANALYSIS

Considering the number of admissions and intubated patients annually in the unit, a population of 73 patients was deemed sufficient to achieve a statistical power of 85%.

Qualitative variables (age, sex, PRISM score, and need of reintubation) were evaluated using the Goodman test for contrasts of proportions among multinominal populations, while quantitative variables (length of stay in the PICU and mechanical ventilation parameters, blood gas levels and endotracheal tube characteristics) were evaluated using Student's t-test when they followed a normal distribution and the nonparametric Mann-Whitney U test otherwise. Odds ratios were calculated to identify the chance of a risk factor being present or not in extubation failure. All analyses were carried out considering a 5% significance level.

RESULTS

During the study period, 383 patients were admitted to the pediatric intensive care unit, of which 179 (46.7%) were intubated and 70 (18.3%) were extubated within 48 hours of admission, leaving 85 patients eligible to join the study. Figure 1 shows the allocation of patients in the study.

[Eligible patients (n = 179) | Did not meet inclusion criteria (n=204) | Excluded (n=94); extubation < 48 hours (n: 70); Death (n: 8); Inaccurate data (n: 4); Prior use of steroids (n: 9); Tracheostomy (n: 3)]

More than half of the patients analyzed were male infants kept on average for four days on mechanical ventilation and six days in the intensive care unit. Table 1 describes the patients included in the study.

Most of the intubations were caused by acute respiratory failure secondary to pneumonia and bronchiolitis. The majority of the patients were intubated with a 4.5 mm endotracheal tube without a pilot balloon (59; 69.4%). Fourteen children (16.5%) were intubated outside the PICU (emergency room, outpatient clinic or operating room) and 71 (83.5%) were intubated after admission to the unit. Sixty-two (72.9%) were intubated on the first attempt. Twenty-seven patients (31.7%) had the tube replaced at least once, either by accidental extubation, obstruction by secretion plug or intense leakage in tubes without a pilot balloon. Diagnosis at admission and causes of intubation are shown in Table 2.

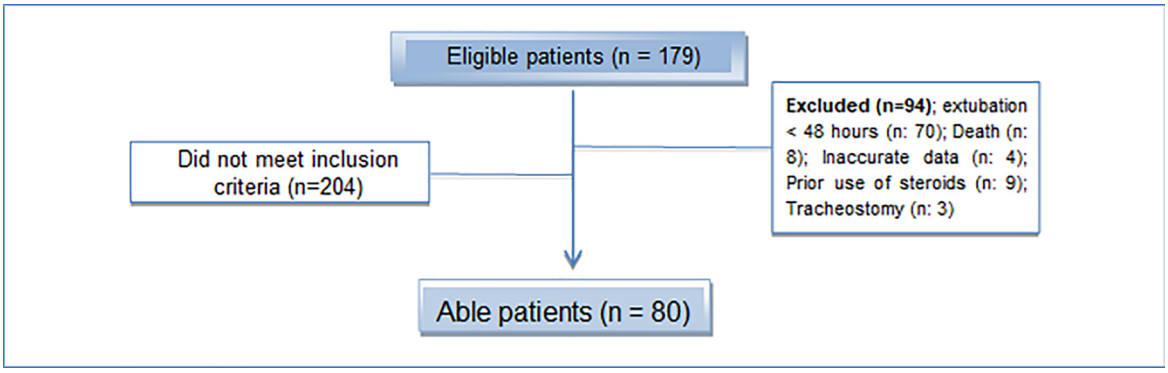


Figure 1. Patient inclusion and exclusion criteria. n = number of patients].

Table 1. Characteristics of the patients included in the study (n=85).

Variables	Results
Age	> 29 days < 3 months: 25 (30%) < 2 years: 37 (43%) > 2 years: 23 (27%)
Sex	
Male	46 (54%)
Female	39 (46%)
PRISM score (mean)	6.14 (4.48)
Time on MV (mean, days)	6.09 (4.18)
COMFORT score	25.6 ± 4.85
ICU length of stay (mean, days)	7.77 (6.63)

PRISM: Pediatric Risk of Mortality; MV: mechanical ventilation

Table 2. Diagnosis at PICU admission and causes of intubation

Diagnosis on admission (n: 85; 100 %)	Causes of intubation (n: 85; 100%)
Pneumonia (43; 50.5%)	Acute Respiratory Failure (58; 68.2%)
Acute Viral Bronchiolitis (13; 15.3%)	Shock (9; 10.5%)
Shock (10; 11.7%)	Surgery (6; 7.1%)
Postoperative complication (6; 7.1%)	Head Trauma (6; 7.1%)
Head Trauma (6; 7.1%)	Status epilepticus (5; 5.9%)
Status epilepticus (5; 5.9%)	
Acute Liver Failure (1; 1.2%)	Hepatic Encephalopathy (1; 1.2%)
Acute Viral Laryngitis (1; 1.2%)	

Twelve of the 85 (14.1%) included patients were less than three months old; two (2.3%) were on mechanical ventilation for more than 15 days; ten (11.7%) had an oxygenation index greater than 10 at some point during hospitalization; 51 (60%) had hypercapnia (defined by an increase in partial pressure of carbon dioxide above 45 mmHg); 18 (21.1%) developed shock; 12 (14.1%) used vasoactive drugs for more than 48 hours; 14 (16.4%) developed acute respiratory distress syndrome (ARDS); and four (4.7%) had cardiac arrest.

Patients were extubated after undergoing spontaneous breathing trials. Support pressure was adjusted to provide a tidal volume of 4 to 6 mL/kg, positive end-expiratory pressure of 5 cmH_2O, and an FiO_2 below 0.5. Subsequently, the patients remained for 60 minutes in the PS ventilator mode, with previously specified parameters, on continuous assessment of vital signs, breathing (intercostal or subdiaphragmatic retractions and nasal flaring), and respiratory mechanics (tidal volume, respiratory minute volume, respiratory rate, dynamic compliance, and muscle strength) captured on the mechanical ventilator screen and capnography. Patients without alterations in the parameters evaluated during the trials were considered suitable for extubation.

After extubation, 11 patients (12.9%) were reintubated within less than 48 hours and three (3.5%) immediately after they had been extubated. The variables extracted from the questionnaire were analyzed. The ones occurring more frequently in patients with failed extubation are listed below. Table 3 shows the comparison between patients with failed (n: 11) and successful (n: 74) extubation.

DISCUSSION

Conventional mechanical ventilation is the ventilatory support mode often used to maintain pulmonary function while the cause of intubation is reversed. Endotracheal intubation is required in mechanical ventilation, although it may produce important complications, especially in the upper airways, which may occur immediately or within the first 48 hours of extubation. Failure to promptly address complications may cause severe sequelae[11,12].

Studies involving intubated children to assess predictors and risk factors associated with extubation failure are not common, and most have included small populations. Extubation failure was observed in 12.9% of our population, a result in line with most of the literature about children on mechanical ventilation [2-7,9,12,18-19].

Laryngeal stridor and post extubation laryngitis are among the main causes of extubation failure. Inflammation of the upper airway may result from inadequate intubation maneuvers and ischemic or mechanical injury, which primarily compromise the subglottic region. As seen in our study, extubation failure is frequently observed in younger patients, especially newborns and infants. This is mainly due to the narrower airways, lower lung and supporting cartilage compliance, and poorly developed collateral ventilation channels (canals of Lambert channels and pores of Kohn) seen in young children [5,6,9,13].

Prolonged mechanical ventilation is an important cause of extubation failure and a major cause of diaphragm dysfunction, affecting up to 50% of adult patients. Prolonged immobilization results in decreased myofibrillar protein concentration, degradation and anomalies in contractile proteins leading to myopathy for muscle disuse and muscle atrophy[8,14-16]. In our population, prolonged MV increased the risk of extubation failure by more than seven times, although not statistically when compared with patients who achieved successful extubation.

Spontaneous breathing trials were performed in all patients before extubation. According to the literature, failure is more frequent when trials are not performed or when patients are unable to not succeed at them. Kurachek et al. reported that 40% of the patients who failed extubation presented inadequate muscle strength and pulmonary dysfunction, alterations recognizable before extubation when adequate weaning protocols are applied. Other authors have found that spontaneous breathing trials predict extubation success, but cannot distinguish which patients might require reintubation after withstanding a spontaneous breathing trial[17-22].

The oxygenation index (OI) is an important predictor of severity that reflects the degree of lung impairment and the aggressiveness of prescribed mechanical ventilation[7]. In our study, OI was higher in patients with failed extubation. This difference, however, was not significant when compared to patients were extubated successfully. Johnston et al. found that children on mechanical ventilation for three days or longer with an oxygenation index (OI) ≥ 5, an expiratory minute volume less than or equal to 1.7 mL/kg/min, a partial pressure ox oxygen (PaO2) ≤ 64 mmHg, a maximal inspiratory pressure (Pimax) ≤ -53 cmH2O, and load-to-power ratio (LFR) > 8, were more likely to experience extubation failure[10].

The administration of vasoactive drugs after cardiorespiratory arrest and shock generates an imbalance between oxygen supply, diffusion and oxygen extraction by tissues in patients on mechanical ventilation, intensifying hypoxia and anaerobic metabolism. As ventilatory support is withdrawn, the cardiorespiratory system has to withstand a sudden change in cardiopulmonary physiology resulting from the removal of positive pressure and the increased ventilatory load on respiratory muscles. Our results showed that shock and ARDS were more frequent in patients with failed extubation (p: 0.0448 and 0.0154, respectively)[23-24].

Most patients admitted to the PICU require sedation and analgesia to optimize treatment and prevent unplanned

Table 3. Factors frequently present in patients with extubation failure.

Variables	n: 11 (12.9%)*	n: 74 (87.1%)	*p*-value	Odds Ratio (95% CI)
Age < 3 months	3	12	0.1834	2.71 (0.54; 7.14)
Mechanical ventilation > 15 days	1	2	0.2434	7.30 (0.42; 126.14)
OI > 10 during hospitalization	2	10	0.6115	1.83 (0.34; 10.02)
Hypercapnia (PaCO2 > 45 mmHg)	5	51	0.3349	0.51 (0.14;1.82)
Shock	4	18	0.2347	2.45 (0.63; 9.53)
Vasoactive drug > 48 hours	4	12	**0.0448**	4.71 (1.13; 19.72)
ARDS	5	14	**0.0154**	6.02 (1.52; 23.84)
Cardiorespiratory arrest	2	4	0.0796	8.00 (1.00; 63.96)
Tube replacement	5	27	0.3147	1.97 (0.54; 7.13)

* Patients with extubation failure presented more than one of the analyzed variables.

extubation. Inadequate sedation and analgesia and endotracheal tube replacement during hospitalization were associated with increased extubation failure rates. Comfort scale scores were calculated twice a day, and our patients achieved a mean score was 25.6 ± 4.85. Similar scores were seen in patients with failed and successful extubation. Despite these precautionary measures, 31% of our patients had endotracheal tubes replaced. The Comfort scale assesses eight parameters, two physiological (blood pressure and heart rate) and six behavioral (alertness, calmness/agitation, respiratory response, physical movement, muscle tone and facial tension). Each parameter is scored from 1 to 5 according to the assessment of the behaviors exhibited by the patient. The total score ranges from 8 to 40, with scores of 17 to 26 generally indicating adequate sedation and analgesia[25-26].

Regarding hypercapnia, Mokhlesi et al. showed that elevated partial pressure of carbon dioxide ($PaCO_2$) was one of the most sensitive predictors of unsuccessful extubation. However, we could not see a relationship between increased $PaCO_2$ and extubation failure in our population [9,27-29].

CONCLUSION

Patients aged of three months or less, spending more than 15 days on mechanical ventilation, shock, use of vasoactive drugs, cardiac arrest, and endotracheal tube replacement increased the risk of extubation failure in our population.

STUDY LIMITATIONS

Although our results were similar to those of other studies available in the literature, the small number of patients analyzed and the lack of a control group may have interfered with extubation failure rates and associated risk factors. In view of the heterogeneity of this group of patients and the omnipresence of extubation failure in pediatric intensive care units all over the world, randomized clinical trials, with controlled variables and patients subdivided in subgroups for age are needed.

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