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Original Article

Incidence of Mechanical Ventilation Adverse Events in Critically Ill Children in a Tertiary Pediatric Intensive Care Unit

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Abstract

OBJECTIVE: Despite the clinical use of mechanical ventilation having well-documented benefits, it can be associated with complications and adverse physiological effects that can impact mortality rates. There are few studies that examine complications associated with mechanical ventilation in children and the factors associated with complications in detail. This study aimed to investigate adverse events associated with mechanical ventilation in pediatric patients and to compare the epidemiology of complications associated with mechanical ventilation.

MATERIAL AND METHODS: The medical records of patients in a tertiary care pediatric intensive care unit who were mechanically ventilated between January 1, 2013, and July 31, 2017, were evaluated.

RESULTS: A total of 187 patients were included in the study, 105 boys (56.1%) and 82 girls (43.9%), and 45 (24.1%) patients experienced complications. The total number of mechanical ventilation days was 1100. Atelectasis (12.3%), post-extubation stridor (8.5%), ventilator-associated pneumonia (5.4%), and pneumothorax (5.4%) were most commonly observed complications.

CONCLUSION: Complications of mechanical ventilation in the pediatric population still occur frequently. In this study, the incidence of atelectasis was high, and also, incidences of ventilator-associated pneumonia and pneumothorax were low.

KEYWORDS: Children, complication, mechanical ventilation, outcome
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INTRODUCTION

Invasive mechanical ventilation (MV) is a frequently applied therapy in the pediatric intensive care unit (PICU) for critically ill children.[1] This therapy is successfully applied in several diseases that lead to respiratory failure, such as respiratory diseases, circulatory failure, septic shock, and central nervous system (CNS) diseases. Despite the clinical use of this technique having well-documented benefits, it can be associated with complications and adverse physiological effects that can impact mortality rates.[1-5]

Studies evaluating the complications accompanying MV in children are rare and were conducted mostly before the use of protective ventilation strategies for acute lung injury.[6,7] Recent studies on children have either been limited to certain complications such as ventilator-associated pneumonia (VAP) and extubation failure (FE) or shared experiences related to non-invasive or home mechanical ventilation for children.[8-10] There are few studies in the literature that examine complications associated with MV in children and the factors associated with complications in detail.[11] Thus, the aim of this study was to investigate adverse events associated with MV in our single-center tertiary PICU and to compare our results with previous studies.

MATERIAL AND METHODS

Intensive Care Unit Features

We had 10 beds and 10 mechanical ventilators (2 Avea, 5 Engstrom CareStation, 1 Hamilton Galileo, and 2 Hamilton C-2) in our PICU. Our unit is a tertiary PICU, an average of 340 patients are hospitalized annually and approximately 16.1% of the patients need MV. The decision to administer MV was made by the responsible PICU physician.

Design

We retrospectively evaluated the medical records of patients who were mechanically ventilated in the PICU during a follow-up period between January 1, 2013, and July 31, 2017.

Patients were eligible for study enrollment when they were between 1 month and 18 years of age and had been ventilated in the PICU for more than 24 hours. Newborn babies were excluded from the study because the neonatal intensive

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care unit was separated. Three patients with chronic respiratory failure, who could not be sent home because of a lack of socioeconomic means and long-term MV treatment (590, 426, and 393 days), were excluded from the study to avoid affecting the mean duration of hospitalization and follow up time on MV.

The patients' medical records were retrospectively reviewed to collect the following data: age, gender, length of stay in the PICU, primary diagnosis of patients, length of MV treatment, complications accompanying MV, underlying primary diseases, comorbid conditions, and outcomes.

The primary diagnosis was done by dividing the patients into 4 groups: respiratory diseases (pneumonia and bronchiolitis), cardiovascular diseases (heart failure and circulation failure), CNS diseases (meningitis, encephalitis, coma, and status epilepticus), and severe sepsis or septic shock.

The pediatric risk of mortality (PRISM) scores of all the patients were measured at admission to determine the severity of the disease, predict recovery from illness, and evaluate the performance of our PICU. Pediatric logistic organ dysfunction (PELOD) scores were also measured in subjects who had organ failure.

Definitions

Chronic respiratory failure in an infant or child was defined as a continued requirement for mechanically assisted ventilation, part-time or full-time, after attempts to wean for at least 1 month (during which the child was otherwise medically stable) had failed.[12]

Multiple organ failure was established based on the criteria from several works by Wilkinson and Proulox.[13,14] Multiple organ dysfunction syndrome was defined as the simultaneous occurrence of dysfunction in 2 or more organs. We grouped patients with organ system failure as follows: respiratory, cardiac, hematologic, neurologic, renal, and hepatic; patients could qualify for 1 or more of these categories. The respiratory failure criteria were hypoxia (pO_2 < 50 cmH_2O), sudden CO_2 retention (pCO_2 > 50 cmH_2O), and SO_2 < 90%.

Sepsis and septic shock were defined according to the guidelines of the American College of Chest Physicians and Intensive Care.[15]

Looking at the file records, it was seen that VAP was defined as pneumonia that occurs 48-72 hours or thereafter following endotracheal intubation, characterized by the presence of a new persistent infiltrate on chest radiograph, presence of at least 2 clinical infection signs (fever, altered white blood cell count, purulent respiratory secretions, worsening gas exchange), and detection of a causative agent.[16,17] But, Centers for Disease Control and Prevention changed its ventilator-associated events definitions after 2019.[18,19] While the number of patients diagnosed with VAP with old definitions was 13, considering the new criteria, 3 patients were found to have ventilator-associated condition and were excluded from the study.

Acute respiratory distress syndrome was based on the new Berlin definition before June 2015, then the pediatric acute lung injury consensus conference recommendations were considered for diagnosis.[20,21] Extubation failure is defined as reintubation or respiratory assistance needed within 48 hours of a scheduled extubation.[22]

The diagnosis and location of atelectasis were obtained from the records in the file and it was confirmed by looking at the time of file recording and simultaneous chest radiographs.

Statistical Analysis

Statistical Package for the Social Sciences Statistics 17.0 (SPSS Inc.; Chicago, IL, USA) package program was used for the statistical study. The following descriptive statistical methods were applied for data processing: central tendency measures (arithmetical mean and median values), variability measures (variation interval, standard deviation, and interquartile range (IQR)), and relative numbers. The chi-square test was employed in the comparison of categorical variables. The Kolmogorov–Smirnov test was applied to assess the normality of the distribution of continuous data. The Mann–Whitney *U* test was used in the comparison of non-normally distributed data, and these results were expressed as median and IQR. Multivariable logistic regression (LR) analysis (backward LR model) was performed to determine the risk factors associated with complications. A statistically significant difference was defined as *P* value <.05.

MAIN POINTS

- Despite mechanical ventilation (MV) having well-documented benefits, it can be associated with complications and adverse physiological effects that can impact mortality rates.
- Studies evaluating the complications accompanying MV in children are rare and were conducted mostly before the use of protective ventilation strategies for acute lung injury.
- In this study, complications related to MV were examined in detail and compared with a limited number of studies.
- Although changes have been observed in the frequency of MV-related complications over time, complications of MV in the pediatric population still occur frequently.
- In this study, the incidence of atelectasis was higher than in previous studies. Also, the incidences of ventilator-associated pneumonia and pneumothorax were lower than in previous studies.

RESULTS

During the study period, 209 patients were treated with MV (Figure 1). After considering the exclusion criteria, 187 patients were included in the study: 105 boys (56.1%) and 82 girls (43.9%). The total number of MV days was 1100. The median age of the 187 patients was 2 years (IQR = 1-5 years). The median length of stay in the PICU and the duration of MV treatment were 10 days (IQR = 4-18 days) and 6 days (IQR = 2-12 days), respectively (Figure 2). Twenty-eight (14.9%) had chronic underlying diseases. The mean PRISM score was

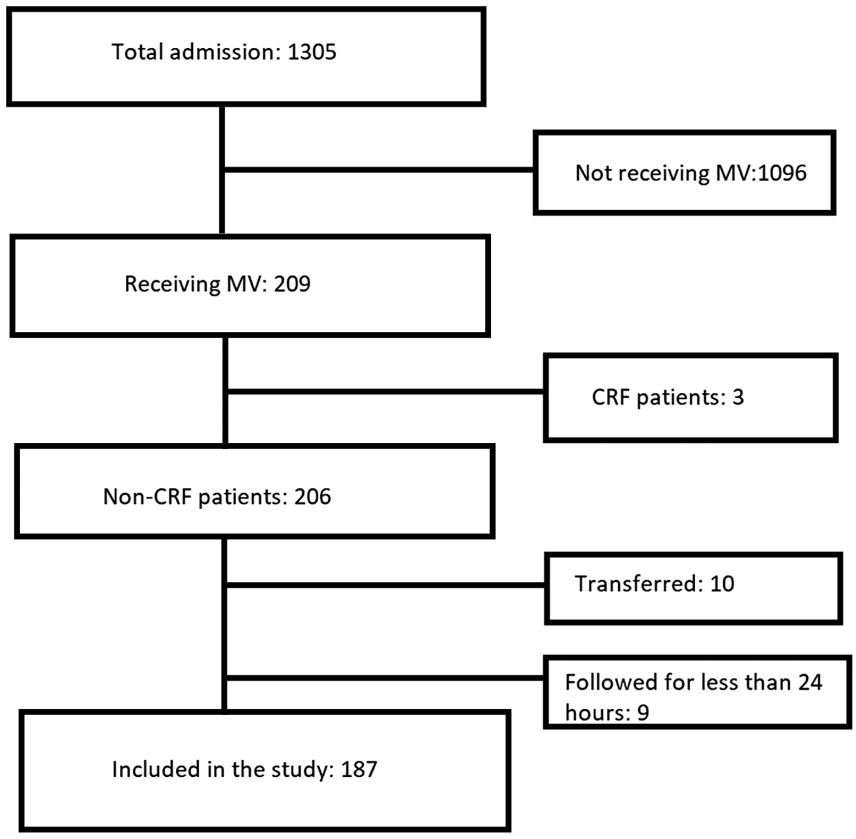

Figure 1. Consort diagram of patients.

18.1 ± 5.9. The mean PELOD score of the patients with organ failure was 21.1 ± 7.4.

Primary diagnoses of patients were divided into 4 groups: respiratory diseases (54.1 %), severe sepsis or septic shock (25.1%), cardiovascular diseases (18.2%), and CNS diseases (11.8%). The most common reasons for intubation were pneumonia (39.1%), septic shock (14.4 %), and heart failure (12.8%) (Table 1).

The mean MV parameters were post-inspiratory pressure (PIP): 20.4 ± 1.2 (cm H_2O), positive end-expiratory pressure (PEEP): 4.3 ± 0.9 (cm H_2O), FiO_2: 0.65 ± 0.1, mean airway pressure (Paw): 10.5 ± 1.1 (cm H_2O), tidal volume (Tv): 5.6 ± 0.9 (mL/kg), and rate: 26.4 ± 4.5 (breaths/min) in the first 24 hours. The maximal values of these parameters during the course of ventilation were PIP: 44 (cm H_2O), FiO_2: 1.0, PEEP: 12 (cm H_2O), and rate: 40 breaths/min for some patients.

Forty-five (24.1%) patients experienced complications related to the delivery of mechanical ventilation (Table 2). Atelectasis was documented on 40 occasions in 23 patients (36 episodes per 1000 days of ventilation) and was detected most frequently (66% of episodes) in the right upper lobe. Post-extubation stridor (PES) was observed in 16 (8.5%) patients (14 episodes per 1000 days of ventilation). These patients

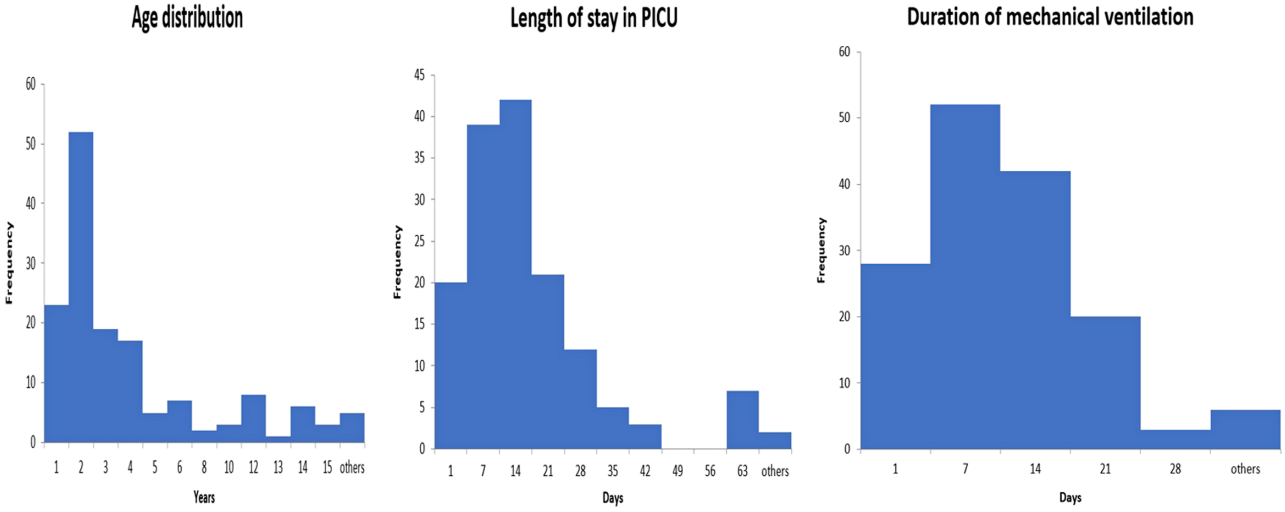

Figure 2. A histogram of patient ages, length of stay in PICU, and duration of mechanical ventilation. PICU; pediatric intensive care unit.

Table 1. Patients Characteristics

Primary diagnosis of patients*	**n, %**
Respiratory diseases	101, 54.1
Pneumonia	73, 39.1
Bronchiolitis	16, 8.5
Other	12, 6.4
Severe sepsis or septic shock	47, 25.1
Septic shock	27, 14.4
Severe sepsis	20, 10.7
Cardiovascular diseases	34, 18.2
Heart failure	24, 12.8
Circulation failure	10, 5.4
CNS diseases	22, 11.8
Meningitis–encephalitis	10, 5.4
Coma	7, 3.7
Status epilepticus	5, 2.7
Outcomes	**n, %**
Death	18, 9.6
Recovery	169, 90.4
Ventilator parameters	**Median (IQR)**
PEEP, cm H2O	5 (4-7)
PIP, cm H2O	22 (18-26)
FiO_2, (%)	60 (40-70)
Tv, mL/kg	5 (4-8)

*Some patients experienced more than one indication.
CNS, central nervous system; Tv, tidal volume.

were treated with nebulized epinephrine and corticosteroids, and 10 (62.5%) of these patients were intubated with a cuffed tube. Although PES was more frequent in patients who used a cuffed endotracheal tube, it was not statistically significant ($P = .08$). Subglottic stenosis was observed in one of the patients who developed PES. The patient was followed up by the otolaryngology clinic. Pneumothorax was documented on 14 occasions in 10 patients (13 episodes per 1000 days of ventilation). Although pneumothorax was usually detected unilaterally, it developed later in 4 patients on the other side. There was no significant relationship between the development of pneumothorax and the presence of chronic respiratory disease. Although there was no difference in initial MV parameters between patients who developed pneumothorax and those who did not, the mean PEEP and PIP values at the time of pneumothorax occurrence were significantly higher than initial MV parameters ($P = .03$). This condition may have occurred as a result of damaged lung tissue and increased pressure requirement over time. Extubation failure occurred in 12 (6.4%) patients (11 episodes per 1000 days of ventilation) and 2 of these patients were hypotonic, 2 had upper airway stenosis, and 1 had a diagnosis of cerebral palsy. Non-invasive ventilation was started in 4 patients in an attempt to avoid repeat endotracheal intubation. The other patients were successfully extubated in the second trial. Of these patients, 2 had impaired respiratory effort and 2 had upper airway obstruction. Additionally, the number of days of neuromuscular blockade and the duration of ventilation were longer in these patients. Ventilator-associated pneumonia was observed in 10 patients (5.4%) (9 episodes per 1000 days of ventilation). Identification of the causative agent for VAP was possible in the 5 cases; *Pseudomonas aeruginosa* (3 cases) and *Staphylococcus aureus* (2 cases) were

Table 2. Observed complications and co-morbidities in patients

	Number of patients,* n (%)	**Complications/co-morbidities per 1000 ventilator days**
Observed complications		
Atelectasis	23 (12.3)	36
Post-extubation stridor	16 (8.5)	14
Failed extubation	12 (6.4)	11
Pneumothorax	10 (5.4)	13
VAP	10 (5.4)	9
Accidental extubation	5 (2.7)	4.5
Nasal or perioral tissue damage	4 (2.1)	4
Vocal cord paralysis	1(0.6)	1
Co-morbidites		
Cardiovascular insufficiency	73 (39.1)	65
Multiple organ failure	31(16.5)	28
Occurence ARDS	17 (9.1)	15
Acute renal failure	16 (8.5)	14
Gastric bleeding	5 (2.7)	4
Thrombophlebitis	3 (1.6)	3

*Some patients experienced more than one complication.
ARDS, acute respiratory distress syndrome; VAP, ventilator-associated pneumonia.

Table 3. Risk factors associated with complications (multivariable logistic regression analysis)

	Beta	Odds Ratio (95% CI)	*P*
Length of stay	−0.028	0.972 (0.942-1.003)	.078
Comorbid diseases	2.354	10.527 (3.576-30.994)	**<.001***
Recurrent hospitalization	1.477	4.381 (1.515-12.668)	**.006***

* $P < 0.05$.

identified as the responsible pathogens. The multivariate logistic regression analyses showed that comorbidities (odds ratio (OR): 10.527, 95% CI: 3.576-30.994, $P < .001$) and recurrent hospitalization (OR: 4.381, 95% CI: 1.515-12.668, $p = .006$) were significantly related to the complications (Table 3).

Several comorbidities were observed in the patients. Multiple organ dysfunction syndrome was observed in 31 (16.5%) patients, 15 (48.3%) of whom died. Cardiovascular insufficiency was observed in 73 (39.1%) patients, 15 (20.6%) of whom died. Acute renal failure was observed in 16 (8.5%) patients, 2 of whom died. Acute respiratory distress syndrome was observed in 17 (9.1%) patients (15 episodes per 1000 days of ventilation), 6 of whom died, despite using protective ventilation strategies. Gastric bleeding (2.7%) was another comorbidity, but none of these patients died (Table 2).

DISCUSSION

This study describes the current prevalence of complications associated with MV in a single tertiary PICU. Sharing experiences on this issue will increase the success of mechanical ventilation applications, and 45 (24.1%) patients experienced complications related to the delivery of MV.

Atelectasis was the most commonly encountered complication in this study (12.4%). Atelectasis was documented on 40 occasions in 23 patients (36 episodes per 1000 days of ventilation). Around 7 % of the atelectasis incidences were reported in some studies that were performed before the use of protective ventilation strategies.[6,7] In studies after the use of protective ventilation strategies reported that this ratio has been increased up to 12.8%-26.3%.[11,23,24] In most of these studies, the frequency of atelectasis is given as percentages. Principi et al[11] reported that atelectasis was observed in 17% of patients (43 episodes per 1000 days of ventilation). Like Principi et al.[11] we considered that the implementation of lung-protective ventilation strategies, with the use of lower PIP and Tv, may contribute to the development of atelectasis. Studies reported that atelectasis was mainly detected in the right upper lobe. This condition may be related to anatomical characteristics of the right upper lobe bronchial orifice and/or higher susceptibility to the adverse effects of suctioning. In this study, atelectasis was detected most frequently (66% of the episodes) in the right upper lobe, consistent with other literature.

The pathophysiology of PES in children is controversial. Despite, some authors have suggested that airway edema secondary to direct upper-airway trauma during intubation or head and neck thermal injuries may lead to PES; others have considered that infections may aggravate mucosal swelling. Furthermore, it has been reported that intubation with a cuffed endotracheal tube does not correlate with the development of post-extubation stridor.[11,25] The PES incidence has been as 2.4%-17% in the literature.[11,24,26-28] Principi et al[11] reported that PES was observed in 13.3% of patients (29.5 episodes per 1000 days of ventilation). The observed PES incidence in this study was 8.5 % (14 episodes per 1000 days of ventilation) consistent with literature. These results suggested that the incidence of PES has not changed over the years.

The rate of VAP is used as a quality indicator for patients receiving MV. However, variable incidence rates were reported across the geographical regions due to several factors, including differences in the diagnostic criteria used, the variable sensitivity and specificity of the available diagnostic tests, and the lack of a gold-standard test for diagnosis of VAP.[29] Highly variable VAP rates (1.9%-34%) were reported in the literature.[11,23,28,30-33] Elward et al[30] reported that the mean VAP rate was 11.6/1000 ventilator days.[27] Principi et al[11] reported that VAP was observed in 1.9% of patients (2.9 episodes per 1000 days of ventilation). The VAP incidence observed in this study was 5.4% (9 episodes per 1000 days of ventilation), similar to the literature. A significant reduction in VAP was reported with the implementation of bundled strategies, such as hand hygiene, elevation of the head of the bed, scheduled mouth care, and changing circuits when soiled.[34] These results suggest that the incidence of VAP has decreased slightly in the last decade. Implementation of bundled strategies may have an effect on this condition. Although we do not have a current protocol for preventing VAP, general protective measures are followed.

Pneumothorax was a relatively common complication of MV (6.8%-13.1%).[11,23] However, the use of lung-protective ventilation strategies appears to reduce the incidence of this complication.[11,24] In a study, this ratio was reported as 2%.[11] In our study, 10 (5.4%) patients experienced a pneumothorax during MV. Other air leaks, such as pneumopericardium or pneumoperitoneum, were not detected in any patients.

Pediatric studies have reported that the incidence of FE has ranged from 6.2% to 14.2%.[20,25,35] Extubation failure has been associated with various conditions, including age ≤ 24 months, dysgenesis conditions, syndromic conditions, chronic respiratory disorders, neurosurgical procedures, prematurity, and congenital heart diseases.[25,35-37] The FE rate was 6.4% in this study. Despite 8 reintubations, which resulted from the increased work of breathing, non-invasive ventilation was started in 4 patients in an attempt to avoid repeat endotracheal intubation. Additionally, the number of days of neuromuscular blockade and the duration of ventilation in these patients were longer than for others. These results suggested that the incidence of FE has decreased slightly in the last decade.

Accidental extubations (AE) occurs at a rate of 0.11-2.27 events per 100 intubation days.[38] Younger patients, inadequate tube fixation, inadequate sedoanalgesia, copious

secretions, and nursing workload are risk factors associated with AE. In a multi-center study, it was reported that significant decreases in AE rates can be achieved with quality improvement.[39] Principi et al[11] reported that AE occurred in 5 patients (0.67 episodes per 100 intubation days) and 2 of whom (40%) required reintubation. The AE incidence observed in this study was 2.7% (0.45 episodes per 100 intubation days), and 3 of these patients (60%) were reintubated.

There are several limitations in this study. Single-center data and retrospective design were the most important limitations. Some data from the file could not be reached. Since data about ventilator-associated tracheobronchitis are not collected, no comment could be made on this subject. Also, since plateau pressure was not saved in most of the files, indexes such as mechanical power and driving pressure could not be used in the study. This was another limitation.

CONCLUSION

Although changes have been observed in the frequency of MV-related complications over time, complications of MV in the pediatric population still occur frequently. These results suggested that the incidences of PES and FE have been similar to previous studies. The incidence of atelectasis in this study was higher than in previous studies, and also, incidences of VAP and pneumothorax were lower than in previous studies.

Ethics Committee Approval: This study was approved by Ethics committee of Adıyaman University, (Approval No: 2017/6-21).

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.K., M.T.; Design – C.K.; Supervision – C.K, M.T.; Resources – C.K., A.K.; Materials – A.K.; Data Collection and/or Processing – C.K., A.K.; Analysis and/or Interpretation – M.T.; Literature Search – C.K.; Writing – C.K. Critical Reviews – C.K., M.T.

Declaration of Interests: The authors have no conflicts of interest to declare.

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