



Clinical Characteristics and Complications of Mechanically Ventilated Children in a Pediatric Intensive Care Unit in Iran: Comparing Different Modes

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Abstract

Background: Mechanical ventilation (MV) is among the most common therapeutic modalities in pediatric intensive care units (PICU), which works based on a defined ventilation mode. Nowadays, conventional and alternative modes including adaptive pressure control (APC) and non-APC modes are frequently employed. Although MV can be helpful in many cases, it may cause some complications resulting in significant morbidity and mortality.

Objectives: This study aimed to investigate the demographic features and complications of mechanically ventilated children in a PICU in Iran, as well as to compare different ventilation modes.

Methods: A retrospective case-control study was conducted in PICUs of children's medical center hospital - a tertiary referral pediatric hospital.

Results: Of 66 patients included in this study, 33 patients were treated with APC modes, whereas 33 patients were treated with non-APC modes. The most common indications for intubation were respiratory failure (53%) and loss of consciousness (13.6%). The mean duration for intubation in patients with and without underlying disorder were 11.7 and 5.2 days, respectively (P -value < 0.01). The means of time for intubation in the APC and non-APC groups were 10 and 11.9 days, respectively (P -value = 0.145). A total of 23 (34.8%) patients had complications, including death, misplacement of the endotracheal tube, atelectasis, unplanned extubation, etc. There was no significant difference between groups regarding the rates of complications, except for atelectasis. Thirteen (19.7%) patients had atelectasis (2 patients in APC group (6%) and 11 patients in non-APC group (33.3%)) (P -value = 0.022). The mortality rate was the same for the both groups (P -value = 1).

Conclusions: In sum, the most common indication for intubation was respiratory failure. No significant difference was observed among patients treated with the APC, and non-APC modes in terms of the complications occurred, except for atelectasis which occurred more frequently in the non-APC group. Therefore, it was concluded that there was no difference between conventional and alternative modes of mechanical ventilation in terms of morbidity and mortality.

Keywords: Atelectasis, Complications, Mechanical Ventilation, Pediatric Intensive Care Units, APC, PRVC, VC+

1. Background

Mechanical ventilation (MV) is one of the most advanced therapeutic options in pediatric intensive care units (PICU) and is repeatedly used to guarantee gas exchange, decrease work of breathing, help the respiratory system and, in some cases, improve underlying disorders (1). The percentage of critically ill children admitted in PICUs annually and in need of MV differs in multiple centers (2-4).

A mechanical ventilator delivers oxygen and elimi-

nates carbon dioxide (CO_2) based on the defined ventilation mode. Conventional modes of mechanical ventilation, including volume control and pressure control, have been used for years and the end results are satisfactory. During improvement or deterioration of the patient condition, however, the operator needs to reevaluate the ventilator setup and the patients frequently, which is time-consuming and requires appropriate expertise. To address this challenge, an alternative mode called adaptive pressure control (APC) was introduced in 1991, which delivered

pressure-controlled breaths while guaranteeing tidal volume (5, 6). According to the results from several original studies, however, no specific mode of mechanical ventilation is superior to another in terms of improving the outcomes and reducing mortality rate (7, 8).

Although mechanical ventilation can be vital for many patients, it may have some complications resulting in an increased rate of morbidity and mortality (9).

2. Objectives

This study, therefore, aimed to investigate the demographic and clinical features of intubated patients treated with MV in PICUs in Iran with a focus on the complications of MV. To the best of our knowledge, the present study was one of the few studies addressing the complications of mechanical ventilation in children based on the applied mode.

3. Methods

In this case-control study, eligible children hospitalized in the pediatric intensive care unit of Children's Medical Center were examined. The given hospital is an academic referral center and the country's center of excellence in pediatrics, located in Tehran, Iran, with all subspecialists available. The pediatric intensive care division in this center has 30 beds. Cardiac and open-heart ICUs are located in separate divisions, which were excluded from our study.

The study was approved by the Research Deputy and Ethics Committee of the Tehran University of Medical Science, under code number 1398.664.IR.TUMS.MEDICINE.REC. A written informed consent signed by patients' parents was obtained at the beginning of admission to the hospital.

All patients aged one month to 16 years and intubated from December 2019 to July 2020 were enrolled in this study. Due to the ongoing covid-19 pandemic, collecting the required data took more time than expected. The exclusion criteria were: (1) presence of other conditions explaining the complications, such as gastrointestinal bleeding in presence of coagulative disorder; (2) presence of complications before initiating mechanical ventilation, such as pneumothorax after bag-mask ventilation; (3) patients with permanent tracheostomy tube; (4) change in mechanical ventilation mode in the course of the disease.

After intubation, the initial mode of ventilation was set based on physician preference, blood gas values, and clinical status of the patient because there was no preferred mode of initial ventilator setup. Sample size was calculated with a power of 90%, in which the least sample size

was approximately 66 patients. The sample size was determined using the following formula:

$$n = \frac{2z_{1-\alpha/2}^2 p(1-p)}{d^2}$$

Of 66 patients included in the study, 33 patients were treated with APC, and 33 ones were treated with non-APC modes. Based on the available ventilator in our center, APC modes were VC+ (Puritan Bennett 840) and PRVC (Siemens Servo-i), and non-APC modes were SIMV/PC/PS, SIMV/PS, and AC/PC. Patients in the two groups had almost identical respiratory failure severity.

A standardized questionnaire was designed based on the study protocol. Demographic data, including age, sex, and weight (for calculation of ideal body weight and ideal tidal volume), disease diagnosis, cause of intubation, and the time of initiation of mechanical ventilation, were extracted from the patient's medical records. During hospitalization, patients were monitored closely by performing pulse oximetry, cardiac monitoring, and serial physical examinations as well as by reviewing vital signs charts. Nasogastric tube (NGT) secretion was also recorded to exclude gastrointestinal bleeding. To prevent ventilator-associated events from turning into pneumonia (VAP), patients were maintained in a semi-recumbent position, and the standard close suction was performed. During hospitalization, all complications were addressed carefully and treated immediately. Complications occurring during this period included upper gastrointestinal bleeding (presence of blood in NGT), post-extubation stridor (lung auscultation with or without stethoscope), subcutaneous emphysema (CXR or palpitation), pneumothorax, and atelectasis (written reports of CXR), VAP (CXR, clinical signs, and symptoms) as well as mini bronchoalveolar lavage and unplanned extubation (clinical observation). The duration of intubation and ventilation mode was also extracted from medical notes.

All statistical analyses were performed using SPSS statistical software (version 24.0.0: PASW, SPSS Inc., Chicago, IL). Estimated odds ratios (ORs) with 95% confidence intervals (95% CIs) and P-values < 0.05 were used to assess the statistical significance of the correlations and associations between indicators. P-value < 0.05 was considered significant. Kolmogorov-Smirnov test was carried out to find normality. Furthermore, chi-squared and Mann-Whitney U tests were applied to compare qualitative and quantitative variables, respectively. Multivariate logistic regression was used to assess the dependency of the achieved outcomes.

4. Results

A total of 75 patients were requested to participate in this study. However, 66 patients were finally enrolled in the study, out of who 33 patients were treated with APC modes and 33 ones were treated with non-APC modes.

The mean age of patients was 46 months and 1 week. Of 66 participants, 21 (32%) were females, and 45 (68%) were males. There were no significant differences in the mean age and gender of the participants in the two groups (P-values = 0.089 and 0.849, respectively).

Sixty two (94%) patients were afflicted with an oral endotracheal tube (ETT), and 3 (4.5%) patients had nasal ETT. One (1.5%) patient had a tracheostomy tube, which was inserted due to a maxillofacial surgery (mandible tumor resection), and was removed after 7 days. Therefore, it wasn't excluded from our study. Also, 61 (92.4%) patients had cuffed ETT, and 5 (7.6%) patients had non-cuffed ETT. There were no significant differences between the two groups in terms of the type of intubation and type of ETT (P-values = 0.999 and 0.926, respectively).

As mentioned earlier, an attempt was made to select patients with almost similar respiratory failure severity in order to prevent the probable bias as much as possible. According to literature, PaO₂/FiO₂ thresholds to stratify the severity of respiratory failure are: Acceptable (PaO₂/FiO₂ > 300 mm Hg); mild (PaO₂/FiO₂ 201 - 300 mm Hg); moderate (PaO₂/FiO₂ 101 - 200 mm Hg); severe (PaO₂/FiO₂ ≤ 100 mm Hg). In general, 27 (41%) patients had no respiratory failure, 17 (25.8%) ones had mild respiratory failure, 7 (10.6%) ones had moderate respiratory failure, and 15 (22.6%) ones had severe respiratory failure. The difference between APC and non-APC groups was not significant in this regard (P-values = 0.655, 0.829, 0.719, and 0.816 for no, mild, moderate, and severe respiratory failure, respectively). The correct selection of patients in the studied groups was supported by this finding. The indications for intubation were respiratory failure (53%), loss of consciousness (13.6%), post-operative (12.1%), seizure (12.1%), and septic shock (9.1%). There were no significant differences between APC and non-APC group in this regard (P-values = 0.682, 0.999, 0.712, 0.267, and 0.675, respectively).

Since this study was conducted in a referral center, 89.4% of patients had an underlying disorder. The duration for intubation in patients with and without underlying disorders were 11.7 and 5.2 days, respectively, which was statistically significant (P-value < 0.01). Irrespective of the underlying diseases, the duration for intubation in the APC group was 10 days, whereas it was 11.9 days in the non-APC group. There was no statically significant difference between the groups in this regard (P-value = 0.145).

Table 1 outlines the baseline characteristics in APC and

non-APC groups. Table 2 shows the distribution of underlying disorders in two groups.

Of 66 patients, 23 (34.8%) ones had complications - 9 (27.3%) from APC group and 14 (42.4%) from non-APC group. In addition, 11 patients had more than one complication. In general, 40 complications were found.

Our recorded complications were death, misplacement of ETT, VAP, pneumothorax, pulmonary hemorrhage, atelectasis, stridor after extubation, emphysema, pneumomediastinum, and unplanned extubation/re-intubation. Table 3 shows the complications of mechanical ventilation in APC and non-APC groups separately. Except for atelectasis, there were no significant differences between the two groups regarding the rate of complications.

Unfortunately, 10 patients from the APC group and 10 ones from the non-APC group expired, and, therefore, no significant difference was observed between the two groups regarding the mortality rate (P-value = 1). Furthermore, 13 (19.7%) patients were afflicted with atelectasis (13.5% in left side and 6% in right side), and 2 (6%) patients in APC group suffered from atelectasis, while 11 (33.3%) patients in non-APC group had atelectasis. The rate of atelectasis was significantly higher in the non-APC group (P-value = 0.022).

Table 4 shows the difference between two groups in terms of the atelectasis rate. It also demonstrates that the only parameter that had an effect on the rate of atelectasis was the mode of mechanical ventilation (P-value = 0.039).

5. Discussion

To the best of our knowledge, this survey was the first one that investigated the children treated with mechanical ventilation in PICUs in Iran. It was also among one of the few studies addressing the complication of mechanical ventilation in children based on the mode in the world.

During the study period, approximately 1000 patients were admitted in CMC's PICUs, 20% of who were treated with mechanical ventilation. Our study enrolled 66 of them, out of who 33 patients were treated with APC modes and 33 ones were treated with non-APC modes. The percentage of critically ill children admitted to PICU and undergone MV varies in different studies and ranges widely in value (2-4).

In the current study, the most common indications for intubation were, first, the respiratory failure which accounted for 53% of the cases, and, second, was neurologic causes (loss of consciousness and seizure). Other causes were post-operative and septic shock. Respiratory failure has been identified by several studies as the leading cause of intubation (2-4, 10); in few studies conducted in more resource-limited countries, however, neurologic

Table 1. Baseline Characteristics in Adaptive Pressure Control and Non-adaptive Pressure Control Groups

Characteristics	APC Group (n = 33)	Non-APC Group (n = 33)	P-Value
Mean age (mo)	55.0 ± 2.1	40.0 ± 1.9	0.089
Gender			0.849
Male	10 (30.3)	11 (33.3)	
Female	23 (69.7)	22 (66.7)	
Type of intubation			0.999
With oral ETT	31 (94.0)	31 (94.0)	
Nasal ETT	1 (3.0)	2 (6.0)	
Tracheostomy tube	1 (3.0)	0 (0.0)	
Type of ETT			0.926
With cuff	30 (91.0)	31 (94.0)	
Without cuff	3 (9.0)	2 (6.0)	
Severity of respiratory failure			
PaO ₂ /FiO ₂ < 100	8 (24.2)	7 (21.2)	0.816
PaO ₂ /FiO ₂ : 101 - 200	4 (12.1)	3 (9.1)	0.719
PaO ₂ /FiO ₂ : 201 - 300	9 (27.3)	8 (24.1)	0.829
PaO ₂ /FiO ₂ > 300	12 (36.4)	15 (45.6)	0.655
Indication for intubation			
Respiratory failure	19 (57.6)	16 (48.6)	0.682
Loss of consciousness	5 (15.2)	4 (12.1)	0.999
Post-operative	3 (9.2)	5 (15.2)	0.712
Seizure	2 (6.0)	6 (18.2)	0.267
Septic shock	4 (12.0)	2 (6.0)	0.675
Duration for intubation (day)			
Without underlying dis.	4.7 ± 0.9	5.7 ± 1.0	0.665
With underlying dis.	10.9 ± 1.2	12.5 ± 1.4	0.775
Total	10	11.9	0.145

causes have been determined as the most common indication for intubation (11, 12). In our study, 89.4% of the patients had underlying disorders, most common of which were neurologic and metabolic disorders in both APC and non-APC groups (Table 2). Our finding in this regard was in contrast to that from the study by Anitha et al. in India (10), suggesting that 24.3% of patients had associated comorbidity, and the neurologic disease and CHD were the major comorbid conditions. This inconsistency in findings may have been attributed to the fact that our study was conducted in one of the most acknowledged pediatric referral centers in our country, where complicated cases from other hospitals were also referred to. To minimize the impact of this confounding factor, an attempt was made to exclude cases in which the underlying disorder itself explained the occurrence of complications.

In our study, the duration of intubation in patients with and without underlying disorders were 11.7 and 5 days, respectively, which was suggestive of a statically significant difference. As for MV mode, duration of intubation in the APC and non-APC groups were 10 and 11.9 days, respectively; however, the difference was not significant. The total duration of intubation, irrespective of other parameters, was 11 days. Farias et al. conducted a prospective cohort study investigating 36 PICUs in 7 countries and showed that 35% of patients received MV for a median time of 4 days (4). In a study by Vijayakumary et al. in Sri Lanka, the duration for intubation was found to be 6 days. They also reported that the main underlying conditions contributing to death were bronchopneumonia and dengue hemorrhagic fever, but they failed to determine the overall rate of underlying disease among the studied population

Table 2. Underlying Disorders in Adaptive Pressure Control and Non-adaptive Pressure Control Groups^a

Characteristics	APC Group (n = 33)	Non-APC Group (n = 33)	P-Value	Total (N = 66)
None	4 (12.0)	3 (9.2)	0.999	7 (10.6)
Immunology	3 (9.2)	3 (9.2)	1.000	6 (9.1)
Neurology	5 (15.2)	12 (36.4)	0.129	17 (25.8)
Pulmonary	2 (6.0)	4 (12.0)	0.675	6 (9.1)
Metabolic	5 (15.2)	5 (15.2)	1.000	10 (15.2)
Oncology	4 (12.0)	1 (3.0)	0.359	5 (7.6)
Dermatology	0 (0.0)	1 (3.0)	0.999	1 (1.5)
Nephrology	4 (12.0)	2 (6.0)	0.675	6 (9.1)
Gastroenterology	1 (3.0)	2 (6.0)	0.999	3 (5.4)
Cardiology	2 (6.0)	0 (0.0)	0.493	2 (3)
Rheumatology	2 (6.0)	0 (0.0)	0.493	2 (3)
Infectious	1 (3.0)	0 (0.0)	0.999	1 (1.5)

^a Values are expressed as No. (%).

Table 3. Complications of Mechanical Ventilation in Adaptive Pressure Control and Non-adaptive Pressure Control Groups

Characteristics	APC Group (n = 33)	Non-APC Group (n = 33)	P-Value
Death	10 (30.3)	10 (30.3)	1.000
Displacement of ETT	7 (21.0)	11 (33.3)	0.403
VAP	2 (6.0)	0 (0.0)	0.493
Bilateral pneumothorax	2 (6.0)	2 (6.0)	1.000
Pulmonary hemorrhage	2 (6.0)	0 (0.0)	0.493
Atelectasis	2 (6.0)	11 (33.3)	0.022 ^a
Stridor after extubation	2 (6.0)	3 (9.2)	0.999
Emphysema	1 (3.0)	1 (3.0)	1.000
Pneumomediastinum	1 (3.0)	1 (3.0)	1.000
Unplanned extubation	1 (3.0)	6 (18.2)	0.113
Re-intubation	1 (3.0)	4 (12.0)	0.359
Total	9 (27.3)	14 (42.4)	0.369

^a Significant (P < 0.05).

(13). These results were inconsistent with our findings regarding the total mean time for MV (11 days), but they were in line with ours regarding the total mean time for MV in patients without underlying disorder (5 days).

One of the main objectives of the present study was to determine the complication of MV. In this regard, it was found that 34.6% of patients had at least one complication, and that the most common complications were death (30.3%) and displacement of ETT (27.3%). Atelectasis and unplanned extubation were also detected to be prevalent among patients from the non-APC group. In this study, the complications were also compared based on the treated mode of MV (Table 3).

The rate of mortality in both APC and non-APC groups was identical, and 30.3% of patients in each group expired despite having been treated with MV. Bhoori et al. conducted a study in 2016 in India and compared the mortality and survival rates in two traditional modes - AC/PC and SIMV PC modes (3). According to their study results, mortality rate in AC/PC mode (47.83%) was significantly higher than that in SIMV PC mode (23.08%) (P-value = 0.0433), and the overall mortality rate was 38.9%. In a comprehensive review by Mireles-Cabodevila et al., alternative modes of MV and their benefits were explored, and some of the theoretical and evidence-based benefits of APC mode, including the guarantee minimum of minute ventilation and less

Table 4. The Difference in Atelectasis Rate in the Multivariable Logistic Regression Model

Parameter	P-Value	Odds Ratio	95% Confidence Interval	
No use of APC	0.039 ^a	5.500	1.131	26.756
Male gender	0.456	0.422	0.379	1.023
Patients' age	0.244	1.256	0.789	1.567
Type of intubation	0.789	1.786	0.986	1.998
Type of tracheal tube	0.223	0.456	0.325	0.789
Severity of failure	0.123	2.266	1.126	4.229
indication for intubation	0.264	0.756	0.666	1.129
Underlying disease	0.129	0.213	0.079	0.456

^a Significant (P < 0.05).

ventilator manipulation by operator, were explained; however, the superiority or inferiority of this mode in terms of mortality was not determined (5). In another expert review by Turner, Rehder, and Cheifetz, the mortality rate among non-traditional modes of MV was discovered to remain unclear (8).

In the present study, the only complication of MV that significantly differed between the two studied modes was atelectasis, which was found in 33.3% of patients in the non-APC group and 6% of patients in the APC group (P-value = 0.022). Overall, 19.6% of our patients developed atelectasis. In order for offering more accurate interpretation of this finding, atelectasis in the multivariable logistic regression model was further analyzed, and it was found that the only factor significantly affecting the atelectasis rate was the mode employed (Table 4). Atelectasis has been recognized by several researchers as a frequent complication of MV; however, the reported rate varies in multiple studies. In the study by Anitha et al., for example, upper lobe atelectasis was determined as the major complication found in 47.4% of the patients (10); while in a study by Mukhtar et al., atelectasis was documented in only 4.6% of the patients, although it was still the most common complication (12). This wide range of atelectasis rates could be partly explained by its pathophysiology. As it is known, atelectasis can be caused by low lung aeration, airway obstruction, and external pressure on the lungs; therefore, the quality of nursing care, such as the frequency of suctioning and the intervals of patient positioning, can directly affect the rate of atelectasis.

5.1. Conclusions

In sum, it was found that the most common indication for intubation was respiratory failure. Most of our patients had underlying disorders, which affected the duration of intubation. There were no significant differences among patients treated with APC and non-APC mode regarding the

observed complications, except for atelectasis which occurred more frequently in the non-APC group. A similar mortality rate was also detected for both studied groups. Therefore, it was concluded that the conventional mode of mechanical ventilation was not generally different from the alternative one in terms of morbidity and mortality.

Footnotes

Authors' Contribution: Study concept and design: M. M.; acquisition of data: T. CH.; analysis and interpretation of data: B. Y.; drafting of the manuscript: M. O.; critical revision of the manuscript for important intellectual content: S. A. H.; statistical analysis: M. SH.; administrative, technical, and material support: Z. N.; study supervision: M. M.

Conflict of Interests: We declare that one of our authors (Dr. M. O.) is a reviewer of this journal.

Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after its publication. The data are not publicly available due to security reasons.

Ethical Approval: The ethics approval code is 1398.664.IR.TUMS.MEDICINE.REC. Link: ethics.research.ac.ir/IR.TUMS.MEDICINE.REC.1398.664.

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Informed Consent: A written informed consent signed by the patients' parents was obtained at the beginning of admission to the hospital.

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