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High-frequency oscillatory ventilation versus conventional ventilation in pediatric patients with acute lung injury: outcomes evaluation

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Abstract

Background: With the development of medical technology and advancements of intensive care units, many types of mechanical ventilators are recruited in the management of acute respiratory distress syndrome (ARDS)/acute lung injury (ALI). We evaluated the outcome of the high-frequency oscillatory ventilation (HFOV) compared to conventional mechanical ventilation (CMV) in pediatric patients with critical respiratory situations mainly ALI or ARDS. A prospective cohort study was performed from 2019 to 2020 in the pediatric intensive care unit (PICU). The following data were recorded: demographic and clinical data, length of PICU stay, mechanical ventilation days, and mortality percentages.

Results: Fifty cases who fulfilled the inclusion criteria were divided into two groups, 24 patients on HFOV from the start and the other 26 were admitted on rescue HFOV after the failure of CMV. There was no statistically significant difference between the two groups regarding the age ($p = 0.571$) and the oxygenation index (OI) ($p = 0.651$). Early HFOV demonstrated shorter length of PICU stay and fewer days on mechanical ventilation. The mortality rate was less with the application of early HFOV compared to rescue HFOV.

Conclusions: Early admission on HFOV can be a safe option in the management of patients with critical lung situation as ARDS/ALI.

Keywords: Acute respiratory distress syndrome, Mechanical ventilation, Pediatrics, PICU

Background

Acute lung injury (ALI) is a sort of acute lung inflammation recognized microscopically with alveolar leukocyte infiltration and protein-rich non-hydrostatic pulmonary edema causing refractory hypoxemia [1, 2]. Acute respiratory distress syndrome (ARDS) is the most severe form of ALI. According to Berlin definition and the American-European Consensus Conference (AECC) in 1994, ARDS is defined through bilateral infiltrates seen on frontal chest radiograph, PaO_2 / $FiO_2 \leq 200$ mmHg and pulmonary artery wedge pressure ≤ 18 mmHg with no evidence of left atrial hypertension [3, 4]. ARDS is caused by variable pulmonary and non-pulmonary causes. It is mostly a complication of infectious pneumonia and sepsis [1] The incidence of ARDS is less common in the pediatric population than adults [5, 6]. The incidence in the pediatric population is reported between 2.2 to 12.8 per 100,000 person-years. From the critical care point of view, ALI/ARDS accounts for 2.2 to 2.6% of PICU admissions [1].

High-frequency oscillatory ventilation (HFOV) was created as a method to provide better lung protection

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during ventilation. HFOV oscillates the lung around a constant mean airway pressure (mPaw) that is higher than that usually applied during conventional ventilation (CV). Although the oscillations may cause significant pressure fluctuations in the endotracheal tube, the pressure fluctuations are significantly attenuated at the alveolar level. Distal maintenance of pressure fluctuation depends on variable factors including respiratory rate, inspiratory duration, endotracheal tube diameter, lung compliance, and lung region (e.g., middle versus upper lobe). Implementation of a constant mPaw during HFOV provides preservation of alveolar recruitment while avoiding low end-expiratory pressure and high peak pressures [7–9].

Currently, the best definitive approach to use mechanical ventilation among the pediatric population has not been settled [10–15]. For this reason, the objective of this study is to compare the outcomes of using either early HFOV or rescue HFOV to reveal the better method to use in the management of ARDS/ALI at PICU.

Methods

This prospective cohort study took place in the Pediatric Intensive Care Unit (PICU) of a tertiary center in Cairo, Egypt. Patients were enrolled from October 2019 to February 2020. Written informed consent was obtained from the parents or guardians of all participants on admission to hospital including the procedures performed during hospitalization. Consent to participate was waived as this study was observational. Ethical approval was obtained from the research ethics board. This study was conducted under the Declaration of Helsinki.

The study subjects were 50 critically ill patients with ALI/ARDS on mechanical ventilation, 24 HFOV, and 26 CMV. The choice of mechanical ventilation mode was according to machine availability at the time of initiation.

Patients' classification was based mainly on the timing of HFOV and their survival. HFOV patients were initially ventilated by HFOV once diagnosed with ALI, not CMV. Rescue HFOV patients managed by HFOV after the failure of conventional ventilation according to the attending physician assessment.

Early HFOV parameters were mean pressure 10 cm H_2O on starting and changed according to oxygen saturation of the patient besides X-ray finding (lung inflation to 9th rib), the frequency was according to age with a range of 6–10 HZ, and the amplitude adjusted according to chest wiggle. According to the applied protocol at the hospital, CMV was assist control with positive end-expiratory pressure (PEEP) 5 cm H_2O, peak inspiratory pressure (PIP) 20 cm H_2O, and FiO_2 40% with target lung recruitment in the form of increasing PEEP and PIP + 2 cm H_2O. Rescue HFOV was initiated after the failure of maintaining O_2 saturation > 85% and failed lung recruitment. Mean pressure was 5 cm H_2O higher than calculated for CMV.

All patients were selected according to AECC Criteria to diagnose ALI/ARDS patients, which includes patients with acute onset, bilateral chest radiographic infiltrates, absence of clinical evidence of left atrial hypertension assessed by bedside echocardiography and impaired oxygenation regardless of positive end-expiratory pressure with a PaO_2/FiO_2 ratio $\leq$ 300 mm Hg for ALI and $\leq$ 200 mmHg for ARDS [16]. According to the Berlin definition, marked lung injury ($PaO_2/FiO_2 \leq 200$) was classified as moderate and severe ARDS, while ALI ($PaO_2/FiO_2 \leq 300$) was classified as mild ARDS [17].

The exclusion criteria of the population included patients having a history of interstitial lung disease, renal failure, malignancy, inborn errors of metabolism, patients with a cardiac lesion, and if their anthropometric measures were below or above 5th and 95th, respectively. We applied these criteria to limit confounding factors that may affect the outcomes under investigations.

HFOV was performed using SLE5000 (Croydon CR2 6PL UK) according to body weight. All patients were sedated with continuous intravenous infusion of midazolam 1 μg/kg/min and fentanyl 1 μg/kg as an analgesic at the time of applying mechanical ventilation. Prone position, neuromuscular blockers, and inotropes were not used.

All patients enrolled in this study were exposed to detailed medical history, complete clinical examination, scoring of critical illness using Pediatric Logistic Organ Dysfunction (PELOD) score at the time of starting ventilation by a physician who was blinded to the group to which the patient belonged, oxygenation index (OI) measurement defined as $(mPAW \times FiO_2 \times 100)/PaO_2$, ventilatory management, chest X-ray to diagnose ALI/ARDS, assessment of the length of stay in PICU, and the duration of mechanical ventilation in both survivors and non-survivors.

Statistical analysis

Data were expressed as the mean and standard deviation in normally distributed continuous variables and as median and standard deviation if skewed. *T* test method was used to compare 2 independent groups' means. Fisher's exact test was used to check the difference between categorical variables. *P* value was always set at 0.05, and all statistical manipulation and analyses were performed using the Statistical Program for Social Science (SPSS Inc., Chicago, IL, USA) Version 16.0 for Windows.

Table 1 Baseline characteristics of patients

Characteristic	Early HFOV ($N = 24$)	Rescue HFOV ($N = 26$)	*P* value
Age, median (Q1–Q3), m	14.5 (3–48)	10 (6–48)	0.571
Sex			
Male	20 (71.4%)	8 (28.6%)	
Female	4 (28.6%)	18 (81.8%)	
PELOD	9.5 ± 1.28	9.5 ± 0.6	1
Oxygenation Index	218.7 ± 35.4	201.9 ± 53.8	0.651

Values are presented as *n* (%) or median (IQR1-IQR3). *P* value using chi-square test and Mood's median test

Table 2 Number and diagnosis of excluded cases despite having ALI/ARDS

	Interstitial lung disease	Malignancy	Inborn metabolic diseases	Renal	Cardiac	Total
Number	15	4	2	11	9	40
Percentage	37.5	10	5	27.5	22.5	100

Table 3 Diagnosis of cases put on mechanical ventilation

	Early HFOV ($N = 24$)	Rescue HFOV ($N = 26$)
Pulmonary	0	4
Non-pulmonary	24	22

Results

The pediatric patients with ALI/ARDS were 50 cases who met the inclusion criteria, 24 were put on early HFOV from the start, while 26 used rescue HFOV after the failure of CMV There was no significant difference as regard age, PELOD and oxygenation index in either group at admission as shown in Table 1.

Table 2 demonstrates the cases excluded according to the defined criteria. Table 3 presents causes of admission which were completely non-pulmonary with early HFOV such as sepsis due to gastroenteritis with severe dehydration or encephalitis and represented the majority (85%) of rescue HFOV.

Table 4 compares outcomes between early and rescue HFOV. As regards the length of stay at PICU, early HFOV was effective in reducing the days spent at PICU compared to rescue HFOV. Also, early HFOV minimized days needed on mechanical ventilation. The rate of mortality was significantly lower using early HFOV (50%) than rescue HFOV (84.6%).

Discussion

Our study showed a comparison between HFOV and CMV in critically ill pediatric patients with ALI/ARDS in PICU. After the patients met the inclusion criteria, the twenty-four patients who were put on early HFOV mode showed significant improvement in the mortality outcome and reduction of the needed mechanical ventilation days. Therefore, patients who were admitted on HFOV first showed noticeable improvement than patients who were admitted on CMV then HFOV, i.e., rescue HFOV.

As regards total mechanical ventilation days in PICU, there was significantly lower mean mechanical ventilation days among early HFOV patients compared to rescue HFOV patients. In a study by Gupta, the length of mechanical ventilation was significantly lower in early HFOV patients than late therefore shorter stay

Table 4 Outcome measures

Characteristic	Early HFOV ($n = 24$)	Rescue HFOV ($n = 26$)	*P* value
Length of PICU stay[a]	10.3 ± 5.6	17.3 ± 6.04	< 0.001[b]
Mechanical ventilation days	5.29 ± 3.04	17.3 ± 6.65	< 0.001[b]
Mortality N (%)	12 (50%)	22 (84.6%)	0.014[c]

Values are presented as *n* (%) or mean ± SD

[a] Length of stay in days

[b] *P* value using *T* test

[c] *P* value using Fisher's exact test

in PICU [18]. A study demonstrated that there was no statistically significant difference between the HFOV and CMV groups for a total length of ventilation days' WMD − 2.00, 95% CI − 18.36 to 14.36; and WMD 2.00, 95% CI − 6.55 to 10.55 for the child and adult trials, respectively [19].

CMV group demonstrated deteriorating respiratory function compared to early HFOV group. Therefore, we decided to replace the CMV with rescue HFOV. Following 6 h of early HFOV application, patients showed improvement detected by ABG parameters (PaO_2 increased) and lower required mPAW and FiO_2 leading to decreased OI. We assume that increasing OI was associated with higher mortality in rescue HFOV patients. This assumption was also supported by another retrospective electronic medical record data review which stated that the risk of mortality increased 3 folds with the increase of the maximum point of OI [20]. Sud reported the effects of OI and $PaCO_2$ which did not significantly differ between HFOV and CMV as high mPAW was applied during HFOV [21].

Regarding mortality, early HFOV patients (50%) were survivors while 84.6% of rescue HFOV patients died, and the difference was significant. This suggests that early shift to HFOV has better outcome in pediatric patients with ARDS because of less duration of mechanical ventilation, ventilator-induced lung injury, nosocomial infection, and fewer hospital stays leading to reduced morbidity and mortality. Arnold reported that mortality was only 6% ($n = 1/17$) in patients who were exclusively managed on HFOV, whereas it was 42% ($n = 8/19$) for patients who failed CMV and were transitioned to HFOV. In addition, mortality in patients who were exclusively managed with CMV was 40% ($n = 4/10$) [22]. Another study revealed that the survival rate was approximately 80% in a study of 10 children who used HFOV as an early rescue therapy after a median length of 4 h of CMV. HFOV, as early rescue therapy, minimizes the risk of pulmonary injury by CMV [23]. On the other hand, a study by El-Nawawy showed that there was no significant difference between patients admitted on HFOV and CMV regarding mortality [24]. Although a study mentioned that patients admitted on HFOV showed a high mortality rate thus worse outcome than patients admitted on CMV, but that study was retrospective missing randomization and lost data on specific key variables [18].

In the present study, the mean length of PICU stay was lower among early HFOV patients compared to rescue HFOV patients. Longer PICU stay is associated with exposure to more complications.

Twenty-eight patients participated in our study. Flori reported in a prospective study that there was a similarity between children and adults with ALI which is the lack of influence of gender on the duration of mechanical ventilation or mortality. This is an interesting finding as male newborns, in particular premature infants, share independently increased risk of death, respiratory distress syndrome, and bronchopulmonary dysplasia in multivariate analyses [25].

Given this low sample size in one center, we were not able to exclude type 2 error, and this requires further research to check the validity of results. According to patients' availability at the time of study, it was noticeable that the median age of included population was high compared to average ages seen in PICUs and their diagnosis was mainly non-pulmonary diseases. To the best of our knowledge, no comparable studies discussed the length of PICU stay and HFOV in pediatrics.

Conclusion

Applying the patients on HFOV from the start has a good impact on patients with ARDS/ALI which was accompanied by reducing mortality and morbidity in the ICU. Further studies will be needed to compare early and rescue HFOV in PICU and the availability to use HFOV as an early strategy in lung distress.

Abbreviations

AECC: American-European Consensus Conference; ALI: Acute lung injury; ARDS: Acute respiratory distress syndrome; CMV: Conventional mechanical ventilation; HFOV: High-frequency oscillatory ventilation; mPAW: Mean airway pressure; PEEP: Positive end-expiratory pressure; PELOD: Pediatric Logistic Organ Dysfunction; PICU: Pediatric intensive care unit; PIP: Peak inspiratory pressure; OI: Oxygenation index.

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Authors' contributions

AR has put the study design and collected data. MA shared in the study design and drafting of the manuscript. MH performed the statistical analysis and shared in drafting of the manuscript. NB analyzed and interpreted the data. AO substantively revised the design and work. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Obtained from Ain shams University, Faculty of Medicine, Research Ethics Board ID number 2018-281-15. Written informed consent was obtained from the parents of each child admitted to pediatric intensive care unit.

Consent for publication

Not applicable.

Competing interests
The authors declare that they have no competing interests.

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