High-Frequency Oscillatory Ventilation for Patients during Exudative Phase of Severe ARDS

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Background: *High frequency oscillatory ventilation (HFOV) is theoretically ideal for lung protective strategy ventilation (LPSV) in acute respiratory distress syndrome (ARDS). However, recent studies revealed unsatisfactory outcomes. The authors conducted a study to examine this phenomenon in patients with early phase of moderate to severe ARDS.*

Objective: *To evaluate the effectiveness of HFOV in patients with early phase of moderate to severe ARDS. The primary outcome was 30 days all-cause mortality.*

Material and Method: *The study was a matched-case controlled clinical trial performed in the medical intensive care units, Faculty of Medicine, Siriraj Hospital. The authors compared HFOV with LPSV in adult patients with the early phase of ARDS who received mechanical ventilation less than 72 hours and had moderate to severe hypoxemia (PaO_2/FiO_2 ratio less than or equal 150).*

Results: *Between June 2010 and February 2014, 49 patients with moderate to severe ARDS were included. Fourteen patients who received HFOV were matched with 16 patients who received LPSV. The 30-day mortality in HFOV group was 61.5%; while in control group, 50% ($p = 0.53$). The authors found use of higher doses of sedative drugs and muscle relaxants in HFOV group. In addition, this group had high-level of mean airway pressure (mPaw). The presence of hemodynamic instability was not different in both groups.*

Conclusion: *In adult patients in the early phase of moderate to severe ARDS who received mechanical ventilation for less than 72 hours, HFOV did not decrease the 30-day mortality. Thus, this support should be only a rescue therapy for refractory hypoxemia cases and in highly selected patients.*

Keywords: *Early, Exudative phase, ARDS, HFOV, High-frequency oscillatory ventilation*

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Acute respiratory distress syndrome (ARDS) is a common critical condition which is associated with high mortality (30-60%) despite advanced therapeutic managements[1-3]. Lung protective strategy ventilation (LPSV) as characterized by the use of low tidal volume and positive end-expiratory pressure (PEEP), is currently employed as the standard treatment[4]. This is aimed to protect good parts of lung from alveolar over-distention. However, in severe cases, such supports may not be adequate and may be harmful[5]. High plateau pressures may lead to ventilator-induced lung injury (VILI) and multi-organ dysfunction syndrome (MODS) which later, lead to mortality. Advanced treatment options include airway pressure release ventilation (APRV), high-frequency oscillatory ventilation (HFOV); recruitment strategies, prone positioning, inhaled nitric oxide, and extracorporeal support are introduced. Of these, the one that shares a similar concept to lung protective strategy, is the use of HFOV. This support is characterized by very low tidal volume and respiratory rate in the range of 600 to 900 breaths per minute. Studies in the past demonstrated that HFOV was safe and effective. In 2010, systemic reviews and a meta-analysis compared HFOV with conventional mechanical ventilation. They demonstrated the mortality benefit of HFOV in both of hospital and 30-day mortality. However, two large randomized controlled trials published in 2013 demonstrated no benefit, or even harm, of HFOV in patients with moderate to severe ARDS. These findings brought about the hypothesis that HFOV might be beneficial in patients during the early phase of ARDS and might prevent VILI, MODS and death. Therefore, the authors conducted a randomized controlled trial (RCT) to compare HFOV with LPSV in adult patients with the early phase of ARDS with severe hypoxemia. The measured outcomes of this trial were mortality

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rate, clinical effectiveness and complications of HFOV in this patient population.

Material and Method

Patients

Patients who were admitted to the medical ICU with the diagnosis of ARDS were screened. Since the study was started before 2012, the diagnostic criteria were according to the North American-European consensus conference definition for acute lung injury (ALI)/ARDS[12]. Eligible patients were 1) aged ≥18 year, 2) severity threshold at the time of randomization as one of the followings (modified from 13): A) SaO_2 ≤88% and FiO_2 ≥0.6 on mechanical ventilation with PEEP ≥10 cmH_2O, B) PaO_2/FiO_2 less than or equal 150, C) plateau pressure >25 cmH_2O, D) mean airway pressure (MAP) ≥20 cmH_2O, E) APRV ≥30 cmH_2O, F) patients who continue to deteriorate. Exclusion criteria included cardiogenic pulmonary edema, severe obstructive lung disease, intractable septic shock requiring >15 mcg/kg/min of dopamine or >0.15 mcg/kg/min of norepinephrine, severe air leak, terminal illness and pregnancy.

Consent was obtained for inclusion in the study at the randomization. In patients who were unconscious or sedated, their relatives provided assent on every patient's behalf, and patients were later given opportunity to withdraw from the study.

Ventilator strategies

Patients who were randomized to HFOV received HFOV in the next 72 hours. Detailed methods were previously described[14,15]. HFOV was started at a setting of FiO_2 = 0.6-1.0, oscillation frequency = 5 Hz, inspiratory time = 33%, bias flow = 40 L/min, and MAP = 5 cmH_2O above MAP during conventional ventilation (CV) immediately before conversion to HFOV. Proximal airway pressure amplitude of oscillation (ΔP) was set to achieve chest wall vibration to the level of the mid-thigh. The setting in LPSV group was described in detail in the ARDSnet trail as the group was treated with lower tidal volume[4]. In brief, the tidal volume 6 ml per kilogram of predicted body weight was used. Adjustment of tidal volume (4-8 ml per kilogram of predicted body weight) was possible in order to keep plateau pressure at the level of no more than 30 cmH_2O and to comfort patients with severe dyspnea. PEEP was adjusted according to FiO_2 level. The physiologic targets for the two ventilator treatment arms were similar. The oxygenation target was SaO_2 ≥88% or PaO_2 ≥60 mmHg on FiO_2 ≤0.6. The ventilation target was pH ≥7.15 with $PaCO_2$ <70 mmHg. PEEP, recruitment maneuver and respiratory rate in LPSV as well as MAP, Hz, ΔP and endotracheal cuff leak in HFOV could be adjusted to meet these targets. Bicarbonate therapy could be given for severe acidosis (pH less than 7.15). After 72 hours of study, patients in the HFOV group were switched over to standard LPSV and further adjustment of ventilator setting depended on the ICU team decision. The summary of ventilator procedures was shown in Table 1.

Transitioning back to conventional mechanical ventilation

Once the MAP was reduced to 20 cmH_2O or less and FiO_2 below 0.6 for 6 hours, attending physician would consider the change of ventilator mode from HFOV to CV.

Table 1. Summary of ventilator procedures

	LPSV	HFOV
Initial tidal volume (ml/kg)*	6	-
Initial RR (breaths/minute or Hz)	Adjust for pH > 7.15 (max 35)	5 Hz
Initial PEEP (cmH_2O)**	10	-
Initial MAP (cmH_2O)	-	LPSV + 5
Initial ΔP	-	Adequate chest wall vibration
Initial % I-time	33	33
Ventilation	↑RR (max 35), ↑Tidal volume (max 8 ml/kg)*	↑ΔP, ↓Hz (min 3), Cuff leak
Oxygenation	↑PEEP, ↑FiO_2, ↑% I-time (max 66%)	↑MAP (max 45 cmH_2O), ↑FiO_2

LPSV = lung protective strategy ventilation; HFOV = high-frequency oscillatory ventilation; PEEP = positive end-expiratory pressure; MAP = mean airway pressure; ΔP = proximal airway pressure amplitude of oscillation; % I-time = percentage inspiratory time; RR = respiratory rate; FiO_2 = fraction of inspired O_2

* The tidal volume is based on predicted body weight

** A minimum PEEP of 18 cmH_2O is required before increasing the inspiratory time

General ICU management

Patient care in the ICU was based on the ICU team. Investigators did not involve themselves in general patient care. All medical decisions including sedation use, hemodynamic management, metabolic control, nutritional support, treatment of infection, stomach ulcer prophylaxis, and other adjunctive therapy would be made by the ICU team.

Sedation protocols

Both HFOV and LPSV patients included in this trial received sedation protocol. The former received analgesic drug, sedative drug and neuromuscular blocking agent, while the latter received analgesic and sedative drug elementarily. However, if signs of respiratory distress were noted, they were prescribed with a neuromuscular blocking agent. The drugs that were used in this trial are in the Table 2.

Outcome measurement

The primary outcome was the mortality rate at 30 days. The secondary outcomes were hemodynamic, ventilation and oxygenation changes, dose of sedative drugs and neuromuscular blocking agents, vasoactive drugs, adverse events (including mucus-plugged endotracheal tube, barotraumas, etc.) and 180 day-mortality. Baseline characteristics included sex, age, actual and predicted body weight (kg), Acute Physiology and Chronic Health Evaluation II (APACHE II), Lung Injury Score (LIS), sepsis syndrome, pulmonary infection, air leak, and ventilation pre-study days were recorded. Baseline physiologic parameters before and after randomization at day 1, 3, and 7 were collected as follows: peak inspiratory pressure (PIP), plateau pressure (Pplat), MAP, PEEP, respiratory rate (RR), tidal volume (TV), ΔP, FiO_2, PaO_2, $PaCO_2$, pH, PaO_2/FiO_2, oxygenation index (OI), Simplified Acute Physiologic Score II (SAPS II), heart rate (HR), mean blood pressure (MBP), central venous pressure (if available), pulmonary artery wedge pressure (if available), systemic vascular resistance (if available) and cardiac index (if available).

Definition of adverse event

Tracheostomy: prolong intubation of more than 2 weeks.

Ventilatory failure: arterial blood gas shows pH <7.25 and $PaCO_2$ >50 mmHg during first 3 days of enrollment.

Air leak: new development of pneumothorax, pneumo-mediastinum and subcutaneous emphysema.

Mucous-plugged endotracheal tube: new development of endotracheal tube obstruction.

Ventilator associated pneumonia: new development of pneumonia after intubation more than 48 hours or less than 48 hours after extubation.

Persistent hypotension: use norepinephrine more than 0.5 mcg/kg/hr.

Sample size calculation

The present study was decided to prove the benefit of early use of HFOV, in term of reducing primary outcome, which was mortality at 30 days. From the previous data, the 30 days mortality varied between 46 to 83%[15,16]. In order to detect an absolute risk reduction (ARR) a 20% difference in primary end point (60% to 40%) with a two-sided alpha error of 0.05 and a power of 80%, 200 severe ARDS patients were required for enrollment and randomized into the control and the intervention groups.

Statistical analysis

Patient's baseline characteristics were compared by Chi-square method for the categorical variables and by independent sample t-test for the continuous variables. The comparison of the primary outcome between the conventional and the HFOV groups was performed with the use of an unadjusted Chi-square test. The results were absolute and included relative risks reduction.

Results

Between June 2010 and February 2014, 64 patients were diagnosed as ARDS, of which 49 patients had moderate to severe ARDS. As noted from Fig. 1, we excluded the patients who had mild ARDS and those who were referred from the other

Table 2. Sedative and neuromuscular blocking agent used in study patient

Type	Name	Loading dose	Maintenance dose
Analgesic drug	Fentanyl	0.35-0.5 mcg/kg	1-3 mcg/kg/hr
Sedative drug	Midazolam	0.5-1 mcg/kg	0.7-10 mcg/kg/hr
Neuromuscular blocking agent	Cisatracurium	0.1-0.2 mg/kg	2.5-3 mcg/kg/hr

hospitals. Fourteen patients were included in the randomized controlled trial during the last 2 years. Since the enrollment rate was low, the authors included non-RCT patients. Seven patients who underwent HFOV support by using the same protocol as in the RCT and 9 underwent lung protective strategy ventilation were included. Finally, 30 patients were enrolled in a matched-case controlled clinical trial, 14 patients were in HFOV groups and 16 patients were in control groups. There were no different in baseline characteristics between two groups (Table 3). The severity score, APACHE II, were similar in both groups (27.6±8.0 vs. 26.4±7.3, $p = 0.65$). The causes of ARDS were mostly from pneumonia (71.45 vs. 75%, $p = 0.83$). The patients in both groups were quite strict to lung protective strategy ventilation before randomization (tidal volume (ml/kg) 7.17±3.09 vs. 7.06±2.27, $p = 0.92$).

Clinical outcomes

As noted in Table 4, there was no difference in mortality between HFOV group (64.29%) and control group (50%), $p = 0.43$. In addition, there were no difference in secondary outcomes. Hospital mortality and 180-day mortality were not different (60.0% in HFOV vs. 62.5% in the control group; $p = 0.92$ and 75.0% in the HFOV vs. 76.9% in the control group; $p = 0.91$, respectively). However, we

Table 3. Baseline characteristics

Characteristics	HFOV (n = 14)	Control (n = 16)	*p*-value
Age (year)	50.3±24.3	58.2±13.7	0.29
Sex (% male)	78.6	62.5	0.34
Weight (actual-kg)	62.15±20.8	56.16±12.12	0.38
Weight (predict-kg)	56.38±9.42	56.40±11.26	1.00
Height (cm)	160.64±15.54	161.19±10.43	0.92
Baseline lung injury score			
APACHE II	27.6±8.0	26.4±7.3	0.65
SAP II	53.1±13.6	46.8±10.3	0.18
LIS	3.5±0.5	3.5±0.4	0.67
Cause of ARDS			
Infection			
Pulmonary	71.4	750	0.83
Extra-pulmonary	21.5	25.0	0.79
Non-infection	7.1	0.0	0.28
Baseline vital sign and hemodynamic parameter			
Heart rate (beat/minute)	113.4±12.7	122.0±25.4	0.26
Mean BP (mmHg)	79.1±15.8	75.4±14.7	0.51
Central venous pressure (CVP)	13.1±4.7	14.4±4.0	0.45
Baseline lung mechanics			
Peak inspiratory pressure (PIP)	28.7±6.6	26.4±4.1	0.26
Plateau pressure	29.4±10.9	28.9±4.9	0.93
Mean airway pressure	22.4±9.9	18.2±4.1	0.18
PEEP	13.2±3.7	13.4±2.7	0.85
Tidal volume (ml)	418.1±196.1	391.3±107.8	0.65
Tidal volume/PBW (ml/kg)	7.17±3.09	7.06±2.27	0.92
Respiratory rate (rate/minute)	28.7±6.6	26.4±4.1	0.26
Baseline arterial blood gas			
pH	7.33±0.08	7.26±0.16	0.20
PaO_2	76.1±27.1	90.3±26.3	0.16
$PaCO_2$	48.7±16.6	44.1±17.2	0.47
PaO_2/FiO_2	91.5±36.9	110.0±36.8	0.18
Oxygen index (OI)	18.9±13.3	17.0±6.4	0.62

ARDS = acute respiratory distress syndrome; BP = blood pressure; PBW = predicted body weight

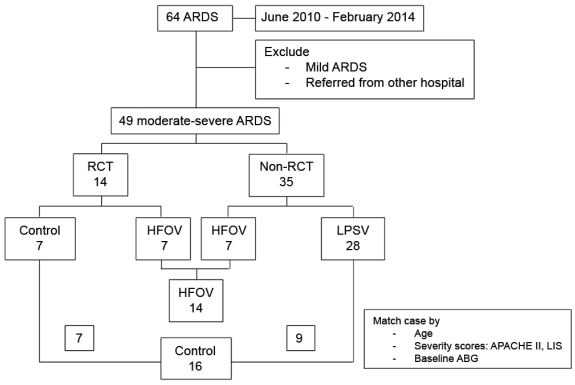

Fig. 1 Flow of the study.

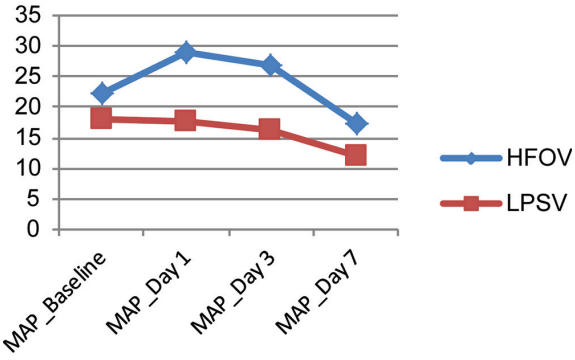

Fig. 2 Mean airway pressure.

found that hypercapnia ($PaCO_2$ >50 mmHg and pH <7.25) was more pronounced in the HFOV group than in control group (21.4% vs. 0% respectively, $p = 0.05$).

According to the use of high MAP in initial setting in HFOV, we found higher MAP in the HFOV than in the control group during day 1 (28.98±9.98 cmH_2O vs. 17.73±4.09 cmH_2O, $p<0.001$), day 3 (26.94±7.76 cmH_2O vs. 16.21±4.86 cmH_2O, $p<0.001$) and this trend had continued higher till day 7 (17.31±7.76 cmH_2O vs. 11.97±4.05 cmH_2O, $p = 0.067$) (Table 4, Fig. 2). However, they did not affect hemodynamic profiles. The uses of norepinephrine were similar in both groups. The uses of midazolam and cisatracurium were significantly greater in the HFOV group than LPSV group during day 1 (midazolam (mg/hr) 4.6±2.8 vs. 1.6±2, $p = 0.002$ and cisatracurium (mg/kg/hr) 0.12±0.08 vs. 0.03±0.04, $p = 0.001$) and day 3 (midazolam (mg/hr) 5.0±2.7 vs. 1.7±3.1, $p = 0.007$ and cisatracurium (mg/kg/hr) 0.13±0.09 vs. 0.03±0.05, $p = 0.001$). The accumulative fluid balance during 7 days was similar in both groups.

Discussion

The result of the present study could be summarized that the use of HFOV in exudative phase of severe ARDS did not improve 30-day and 180-day mortality. Gas exchange parameters, namely oxygenation and ventilation were not better than the standard setting despite higher MAP. Ventilator failure, as characterized by carbon dioxide retention, was noted during HFOV. Also, there were more uses of sedative agents and muscle relaxants in these patients.

The lack of clinical benefit of HFOV in our report paralleled, in some part, with two major studies, the OSCAR trial and the OSCILLATE trial. Both trials were conducted during the same period and reported in 2013, in the same issues of The New England Journal of Medicine. There were certain differences in the study protocols. First, the former was generally aimed to examine the effectiveness of HFOV in ARDS while the latter focused on early phases of ARDS. Second, the set up of MAP in OSCILLATE study employed the use of the initial pressure of 30 cmH_2O while in OSCAR study, the pressure was set pressure of 5 cm of water above the plateau airway pressure at enrollment. Thus, mean HFOV airway pressures in the OSCILLATE study was higher than the control group at protocol initiation (31±2.6 vs. 24±4.0 cmH_2O), and on the next day (28±4.2 vs. 21±4.8 cmH_2O). Our study, although it used the same set pressure as OSCAR study initially, it finally had similar MAP to those in the OSCILLATE trial (Table 5). Airway pressures were higher in the HFOV group from the beginning (22.35±9.94 vs. 18.18±4.08 cmH_2O), day 1 (28.98±9.98 vs. 17.73±4.09 cmH_2O) and day 3 (26.94±7.76 vs. 16.21±4.86 cmH_2O) (Fig. 2). These parameters were different in the OSCAR trial, the control group had slightly higher MAP at the beginning (30.9±11.0 vs. 26.9±6.2 cmH_2O), on day 2 (29.5±10.7 vs. 25.3±5.5 cmH_2O) and on day 3 28.5±11.2 vs. 25.1±5.4 cmH_2O). These could be used as explanation for slightly higher mortality in the HFOV patients, which was comparable to OSCILLATE trial. The other reasons which may explain higher mortality than in the OSCAR and OSCIILATE trials were high APACHE II score, large amount of positive fluid balance in the first 7 days and greater use of benzodiazepine, so these might boost up the mortality rate.

The objective of using HFOV for prevention of VILI might not truly indicate success in this trial because most of our patients had a diagnosis of pneumonia with ARDS with nonhomogeneous lesion,

Table 4. Clinical outcomes

Characteristics	HFOV (n = 14)	Control (n = 16)	*p*-value
Primary outcome			
30 days mortality (%)	64.29	50.00	0.43
Secondary outcome			
Hospital mortality (%)	60.0	62.5	0.92
180 days mortality (%)	75.0	76.9	0.91
ICU length of stay (day)	21.29±18.27	16.63±10.95	0.40
Complication (%)			
Tracheostomy	0	25.0	0.04
VAP	35.7	31.3	0.80
Secretion obstruction	7.1	0	0.28
Pneumothorax	21.4	12.5	0.51
Ventilatory failure	21.4	0	0.05
Hypotension	7.1	6.3	0.92
Mean airway pressure (MAP) (cmH_2O)			
Baseline	22.35±9.94	18.18±4.08	0.137
Day 1	28.98±9.98	17.73±4.09	<0.001
Day 3	26.94±7.76	16.21±4.86	<0.001
Day 7	17.31±7.76	11.97±4.05	0.067
Vasopressors			
Norepinephrine (mcg/kg/minute)			
Baseline	0.09±0.10	0.17±0.16	0.13
Day 1	0.11±0.13	0.19±0.19	0.20
Day 3	0.07±0.14	0.13±0.18	0.42
Day 7	0.02±0.04	0.05±0.12	0.37
Muscle relaxant			
Cisatracurium (mg/kg/hour)			
Baseline	0.09±0.06	0.02±0.04	0.001
Day 1	0.12±0.08	0.03±0.04	0.001
Day 3	0.13±0.09	0.03±0.05	0.001
Day 7	0.04±0.04	0.01±0.04	0.16
Sedative drugs			
Fentanyl (mcg/minute)			
Baseline	83.6±41.3	73.4±26.6	0.43
Day 1	89.3±36.9	68.8±29.6	0.10
Day 3	95.8±41.7	56.3±37.5	0.02
Day 7	75.0±37.8	40.4±42.7	0.08
Midazolam (mg/hour)			
Baseline	4.0±3.0	1.5±1.6	0.007
Day 1	4.6±2.8	1.6±2.0	0.002
Day 3	5.0±2.7	1.7±3.1	0.007
Day 7	3.9±3.2	1.9±2.3	0.12
Accumulative fluid balance during 7 day			
Day 0 (enrollment)	2,148±1,401	3,584±1,754	0.06
Day 1	3,589±2,313	5,659±2,793	0.35
Day 3	4,724±3,782	7,321±5,045	0.18
Day 7	8,075±6,139	8,092±6,372	1.0
New AKI or RRT during 7 days			
RRT (%)	14.23	50.00	0.038

ICU = intensive care unit; VAP = ventilator-associated pneumonia; AKI = acute kidney injury; RRT = renal replacement therapy

Table 5. Comparison of baseline characteristics and primary outcomes to OSCILLATE and OSCAR trial

	OSCILLATE[18]		OSCAR[19]		Our trial	
	HFOV	CMV	HFOV	CMV	HFOV	CMV
No of population (n)	275	273	398	397	14	16
Age (year)	55.0	54.0	54.9	55.9	50.3±24.3	58.2±13.7
APACHE II	29.0±8.0	29.0±7.0	21.8±6.0	21.7±6.1	27.6±8.0	26.4±7.3
PF ratio	121	114	113	113	91.5±36.9	110.0±36.8
TV (ml/kg)	7.2±1.9	7.1±1.8	8.3	8.3	7.17±3.09	7.06±2.27
PEEP	13.0±3.1	13.0±3.3	11.4±3.5	11.3±3.3	13.2±3.7	13.4±2.7
Duration of CV before randomization	2.5±3.3	1.9±2.3	2.2±2.3	2.1±2.2	1.6±1.3	0.38±1.0
In hospital mortality	47%	35%	50%	48%	60.0%	62.5%

CMV = conventional mechanical ventilation; PF = PaO_2/FiO_2; TV = tidal volume; CV = conventional ventilation

Table 6. Hypercarbia and ventilatory failure

	Day 1	Day 3
Our trial		
$PaCO_2$	55.40±24.16	57.91±29.93
Hertz (Hz)	3.53±0.90	3.47±0.79
OSCILLATE		
$PaCO_2$	45.7±15.2	50.7±15.3
Hertz (Hz)	5.5±1.0	6.8±2.0

which allowed less recruitability than extra-pulmonary ARDS[21]. The application of high MAP caused lung over distension in some parts and lung stress and strain thus occurred. This resulted in the exaggeration of VILI. Generally, HFOV generates lower tidal volume that aims to reduce tranpulmonary pressure (less lung stress) and lung injury[23]. However, our trial had limited capability to increase frequency because of hypercapnic respiratory acidosis. Thus, the desired physiologic effects of HFOV were reduced (Table 6).

The limitations of the present study included being a single center research with low enrollment rate. In addition, there was a high proportion of patients with pneumonia.

In conclusion, the use of HFOV in patients with early exudative phase of moderate to severe ARDS who received mechanical ventilation for less than 72 hours did not improve mortality. Evidences of hypoventilation were noted. Some issues need to be clarified; for example, what are the best oscillatory settings, appropriate mean airway pressures and suitable respiratory monitoring which are applied to individual patients. At present, we recommend HFOV as a rescue therapy in refractory hypoxemic cases and in highly selected patients.

What is already known on this topic?

HFOV, theoretically, is the ideal mechanical ventilation to prevent further lung injury from ARDS. But, the benefits of using HFOV in ARDS patients, nowadays, are uncertain. However, it might be useful in moderate to severe ARDS patients and the advantages could be added if we use HFOV in the exudative phase of ARDS.

What this study adds?

HFOV is only a rescue therapy in refractory hypoxemia cases and in highly selected patients. The significant concern points are not only the lung protection but also the balance between hemodynamics and positive pressure, the use of sedation and muscle relaxant, accumulative fluid balance which could improve the outcomes.

Potential conflicts of interest

None.

References

1. Hudson LD, Milberg JA, Anardi D, Maunder RJ. Clinical risks for development of the acute respiratory distress syndrome. Am J Respir Crit Care Med 1995; 151: 293-301.
2. Doyle RL, Szaflarski N, Modin GW, Wiener-Kronish JP, Matthay MA. Identification of patients with acute lung injury. Predictors of mortality. Am J Respir Crit Care Med 1995; 152: 1818-24.
3. Nuckton TJ, Alonso JA, Kallet RH, Daniel BM, Pittet JF, Eisner MD, et al. Pulmonary dead-space fraction as a risk factor for death in the acute respiratory distress syndrome. N Engl J Med 2002; 346: 1281-6.

4. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342: 1301-8.
5. International consensus conferences in intensive care medicine: Ventilator-associated Lung Injury in ARDS. This official conference report was cosponsored by the American Thoracic Society, The European Society of Intensive Care Medicine, and The Societe de Reanimation de Langue Francaise, and was approved by the ATS Board of Directors, July 1999. Am J Respir Crit Care Med 1999; 160: 2118-24.
6. Plötz FB, Slutsky AS, van Vught AJ, Heijnen CJ. Ventilator-induced lung injury and multiple system organ failure: a critical review of facts and hypotheses. Intensive Care Med 2004; 30: 1865-72.
7. Derdak S, Mehta S, Stewart TE, Smith T, Rogers M, Buchman TG, et al. High-frequency oscillatory ventilation for acute respiratory distress syndrome in adults: a randomized, controlled trial. Am J Respir Crit Care Med 2002; 166: 801-8.
8. Bollen CW, van Well GT, Sherry T, Beale RJ, Shah S, Findlay G, et al. High frequency oscillatory ventilation compared with conventional mechanical ventilation in adult respiratory distress syndrome: a randomized controlled trial [ISRCTN24242669]. Crit Care 2005; 9: R430-9.
9. Yoder BA, Siler-Khodr T, Winter VT, Coalson JJ. High-frequency oscillatory ventilation: effects on lung function, mechanics, and airway cytokines in the immature baboon model for neonatal chronic lung disease. Am J Respir Crit Care Med 2000; 162: 1867-76.
10. Imai Y, Kawano T, Miyasaka K, Takata M, Imai T, Okuyama K. Inflammatory chemical mediators during conventional ventilation and during high frequency oscillatory ventilation. Am J Respir Crit Care Med 1994; 150: 1550-4.
11. Imai Y, Nakagawa S, Ito Y, Kawano T, Slutsky AS, Miyasaka K. Comparison of lung protection strategies using conventional and high-frequency oscillatory ventilation. J Appl Physiol (1985) 2001; 91: 1836-44.
12. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. Report of the American-European Consensus conference on acute respiratory distress syndrome: definitions, mechanisms, relevant outcomes, and clinical trial coordination. Consensus Committee. J Crit Care 1994; 9: 72-81.
13. Higgins J, Estetter B, Holland D, Smith B, Derdak S. High-frequency oscillatory ventilation in adults: respiratory therapy issues. Crit Care Med 2005; 33 (3 Suppl): S196-203.
14. Mehta S, Lapinsky SE, Hallett DC, Merker D, Groll RJ, Cooper AB, et al. Prospective trial of high-frequency oscillation in adults with acute respiratory distress syndrome. Crit Care Med 2001; 29: 1360-9.
15. Cartotto R, Cooper AB, Esmond JR, Gomez M, Fish JS, Smith T. Early clinical experience with high-frequency oscillatory ventilation for ARDS in adult burn patients. J Burn Care Rehabil 2001; 22: 325-33.
16. Pachl J, Roubik K, Waldauf P, Fric M, Zabrodsky V. Normocapnic high-frequency oscillatory ventilation affects differently extrapulmonary and pulmonary forms of acute respiratory distress syndrome in adults. Physiol Res 2006; 55: 15-24.
17. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012; 307: 2526-33.
18. Ferguson ND, Cook DJ, Guyatt GH, Mehta S, Hand L, Austin P, et al. High-frequency oscillation in early acute respiratory distress syndrome. N Engl J Med 2013; 368: 795-805.
19. Young D, Lamb SE, Shah S, MacKenzie I, Tunnicliffe W, Lall R, et al. High-frequency oscillation for acute respiratory distress syndrome. N Engl J Med 2013; 368: 806-13.
20. Guervilly C, Forel JM, Hraiech S, Demory D, Allardet-Servent J, Adda M, et al. Right ventricular function during high-frequency oscillatory ventilation in adults with acute respiratory distress syndrome. Crit Care Med 2012; 40: 1539-45.
21. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. N Engl J Med 2006; 354: 1775-86.
22. Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, deBoisblanc B, et al. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006; 354: 2564-75.
23. Goffi A, Ferguson ND. High-frequency oscillatory ventilation for early acute respiratory distress syndrome in adults. Curr Opin Crit Care 2014; 20: 77-85.

การช่วยหายใจด้วยเครื่องช่วยหายใจความถี่สูงในผู้ป่วย acute respiratory distress syndrome

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ภูมิหลัง: การช่วยหายใจด้วยเครื่องช่วยหายใจความถี่สูง (High-frequency oscillatory ventilation, HFOV) ในภาวะ acute respiratory distress syndrome (ARDS) ในทางทฤษฎีแล้วน่าจะเป็นการช่วยหายใจที่มีประสิทธิภาพ เพราะใช้หลักการแบบ lung protective strategies ใช้ปริมาณ tidal volume น้อย แต่ผลการศึกษาในระยะหลังไม่สนับสนุนแนวคิดดังกล่าว

วัตถุประสงค์: เพื่อศึกษาถึงประสิทธิภาพของการใช้เครื่องช่วยหายใจความถี่สูงในผู้ป่วยที่มีภาวะหายใจล้มเหลวระดับปานกลางถึงรุนแรงระยะแรก วัตถุประสงค์หลักคือ อัตราการตายที่ 30 วัน หลังการวินิจฉัยภาวะหายใจล้มเหลว

วัสดุและวิธีการ: การศึกษาแบบ matched case control ในผู้ป่วย ARDS ระยะแรก โดยเปรียบเทียบผู้ป่วยกลุ่มที่ได้รับการรักษาด้วย HFOV กับกลุ่มที่ได้รับการช่วยหายใจแบบ lung protective strategy ventilation (LPSV) โดยเลือกผู้ป่วยที่ได้รับการช่วยหายใจภายใน 72 ชั่วโมง และมีอัตรา PaO_2/FiO_2 น้อยกว่าหรือเท่ากับ 150

ผลการศึกษา: ระหว่างเดือนมิถุนายน พ.ศ. 2553 ถึง กุมภาพันธ์ พ.ศ. 2557 มีผู้ป่วยเข้าร่วมการศึกษา 49 ราย ผู้ป่วย 14 ราย ได้รับการช่วยหายใจแบบ HFOV และผู้ป่วย 16 ราย ได้รับการรักษาแบบ LPSV ผลการศึกษาพบว่า ผู้ป่วยทั้ง 2 กลุ่ม มีอัตราตายที่ 30 วัน ไม่ต่างกัน (61.5% ใน HFOV เทียบกับ 50% ใน LPSV, $p = 0.43$) นอกจากนี้ยังพบว่าผู้ป่วย HFOV ได้รับยานอนหลับและยาคลายกล้ามเนื้อมากกว่า มี mean airway pressure สูงกว่า

สรุป: ในผู้ป่วย acute respiratory distress syndrome (ARDS) ระยะต้น การช่วยหายใจด้วย high frequency oscillatory ventilation (HFOV) ไม่ลดอัตราตายที่ 30 วัน (30-day mortality)