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Hemodynamic effects of high-frequency oscillatory ventilation in severe pediatric respiratory failure

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Abstract *Objective:* To assess the hemodynamic effects of high mean proximal airway pressures (Paw) during high-frequency oscillatory ventilation (HFOV) in non-neonatal pediatrics patients with severe respiratory failure.
Design: Prospective and retrospective study.
Setting: Pediatric ICU in a university-affiliated hospital.
Patients: 8 non-neonatal pediatric patients with severe respiratory failure ventilated with HFOV at our institution between July 1991 and February 1994. All patients had a pulmonary artery catheter.
Interventions: HFOV.
Measurements and results: Higher Paw was required during HFOV to obtain adequate lung expansion during the first 24 h (median 20.9 cmH_2O, range 16.9–30.0 cmH_2O in CMV, versus median 30.0 cmH_2O, range 21.0–33.0 cmH_2O in HFOV, $p = 0.008$), resulting in improved oxygenation as evaluated by alveolar-arterial oxygen difference (median of 557.2 mmHg, range 360.4–607.8 mmHg in CMV, versus median of 410.5 mmHg, range 282.9–550.2 mmHg after 24 h of HFOV, $p = 0.03$). The only observed effect on the cardiovascular system was a decrease in heart rate (median of 162, range 129–178 in CMV, versus median of 142, range 104–195 after 24 h of HFOV, $p = 0.03$). Oxygen delivery, cardiac index, mean systemic arterial blood pressure, and pulmonary and systemic vascular resistances did not change significantly before and after HFOV in the patients as a group, although in one case a decrease in cardiac index and oxygen delivery was observed.
Conclusions: High-Paw HFOV must be used cautiously, but seems to have no discernible adverse effects on the cardiovascular system in most patients.

Key words High-frequency ventilation · Adult respiratory distress syndrome · Artificial respiration · Cardiovascular system

Introduction

Respiratory failure is one of the leading causes of morbidity and mortality in critically ill pediatric patients [1–3]. Although conventional mechanical ventilation (CMV) can provide adequate oxygenation and ventilation in most of cases, certain patients with severe lung injury may need very high mean and peak airway pressures to achieve adequate oxygenation, significantly increasing the probability of death due to progressive barotrauma or long term sequelae.

During high frequency oscillatory ventilation (HFOV), high-frequency low-amplitude pressure oscillations are generated in the airways, while a continuous flow of fresh gas provides for carbon dioxide elimination and main-

tains a mean airway pressure (Paw). HFOV has been used primarily in the treatment of neonatal respiratory distress syndrome. Two clinical trials in premature infants have shown that HFOV can provide effective oxygenation and ventilation [4, 5]. HFOV seems to produce better results, in terms of better oxygenation and lower complication rate, when a high lung volume strategy is used. High pressures during the initial period of HFOV optimize the mean lung volume through alveolar re-expansion, improving gas exchange and reducing the shear stress forces between expanded and collapsed lung units. However, concern exists about the use of high Paw with this strategy which may cause a marked cardiovascular depression and a net decrease in oxygen delivery.

To investigate if high Paw during HFOV will induce cardiovascular depression in critically ill pediatric patients, we studied the changes in mean airway pressure, blood gases, and hemodynamic variables before and after HFOV in a group of non neonatal pediatric patients in which a pulmonary artery catheter had been placed for clinical management.

Methods

The patients were seen between July 1991 and February 1994. We studied the hemodynamic and respiratory data from all non neonatal pediatric patients in whom a pulmonary artery catheter had been inserted for clinical management and who had been ventilated with HFOV. The study has been conducted according to the principles established in Helsinki and was also approved by our Institutional Review Board. Informed consent for using HFOV as an experimental therapy was obtained from the parents in all subjects.

Eligibility for HFOV

Patients were placed in HFOV as a rescue therapy in desperately ill infants and children (3 patients), or as part of a multicenter randomized study comparing CMV versus HFOV in severe respiratory failure (20 patients). Patients were eligible for the randomized study of CMV versus HFOV if they exhibited diffuse alveolar disease with an oxygen index (OI) (O.I. = Paw $cmH_2O \times FIO_2 \times 100/PaO_2$ $mmHg \times 1.4$) of 13 or higher. Rescue patients were evaluated for HFOV using the same criteria before the randomized study was active in our center. All patients were paralyzed with a continuous intravenous infusion of vecuronium. Sedation and pain control were maintained with continuous intravenous infusion of midazolam, and either fentanyl or morphine. All but one patient were receiving at least two inotropic drugs before HFOV was started.

Of the 20 patients placed in HFOV as part of the randomized study, 6 had a pulmonary artery catheter in place at the time HFOV was started. Of the 3 patients placed in HFOV as a rescue therapy, 2 also had a pulmonary artery catheter in place at the time HFOV was started. These 8 patients are considered in this report; their clinical characteristics are depicted in Table 1. Two of these patients had two separate periods of HFOV, but only the first period was used for statistical analysis. (Data from one other patient are not included because information before HFOV could not be collected, even though she was treated for 147 days with good pulmonary results). All patients had severe diffuse alveolar disease (adult respiratory distress syndrome in all cases). Air leak syndrome was present before HFOV in 5 patients. All patients were ventilated with high pressures on CMV for a period ranging from one day to more than 10 days. Only 2 of the 8 patients survived, a fact that reflects our bias toward placement of pulmonary artery catheters only in the sickest patients; this survival rate does not reflect overall survival in HFOV-ventilated patients in our institution, nor is survival the primary outcome of this report. Death was caused by progressive respiratory failure and multiple system organ failure, complicated by progessive air leak syndrome (ALS) in 3 patients. In all cases, death occurred days after initiation of HFOV, except in two cases in whom death occurred approximately 24 h after the study period. Data were collected in a prospective fashion in the six randomized study patients, and in a retrospective fashion in the two rescue patients. The values closest in time to 12 h, 6 h, and 1 h before HFOV, were compared to the values closest in time to 1, 6, 12, 18, and 24 h after HFOV. Before HFOV the patients were ventilated on a Siemens 900C servoventilator (Siemens, Solna, Sweden) on SIMV or volume control mode. The median of the expiratory tidal volumes was 15.3 ml/kg (range 11.0–17.7 ml/kg). The median PEEP was 12 cmH_2O (range 6–14 cmH_2O). At the time of transition to HFOV, all patients were on FIO_2 of 1.0.

Ventilatory strategy for HFOV

The oscillator used was Sensormedics 3100 (Sensor Medics Corporation, Yorba Linda, CA). At the time of transition from CMV to

Table 1 Population characteristics

Patient	Age	Weight (kg)	Diagnosis	Days on HFOV[a]	Outcome
1	8 months	7.5	ARDS[b] unknown origin	13	Survived
2	23 months	10.3	ARDS[b], liver transplant	7	Died
3	14 months	9.7	ARDS[b], septic shock, spinal muscular dystrophy	1.5	Died
4	8 years	35.0	ARDS[b], varicella pneumonitis ALL[c], bronchiolitis obliterans	7 1.5[d]	Died
5	7 years	25.5	ARDS[b], end stage renal failure	2	Died
6	15 months	10.1	ARDS[b], unknown origin	2 29[d]	Died
7	2 years	13.1	ARDS[b], viral pneumonia	7.5	Survived
8	7 years	19.4	ARDS[b], varicella pneumonitis	20	Died

[a] *HFOV* high-frequency oscillatory ventilation
[b] *ARDS* adult respiratory distress syndrome
[c] *ALL* acute lymphocytic leukemia
[d] Second separate period of HFOV

HFOV the FIO_2 was always 1.0. Paw was started 2 cmH_2O above the last Paw on CMV, and then increased as necessary to achieve arterial hemoglobin saturations above 90% and PaO_2 above 50 mmHg. When adequate oxygenation was achieved, FIO_2 was slowly decreased to 0.6, increasing again Paw as necessary to keep the arterial hemoglobin saturation 90% or higher. When the FIO_2 was decreased to 0.6 and the saturation was still 90% or higher, the Paw was slowly decreased as long as an adequate oxygenation was maintained. Frequent chest roentgenograms were obtained to detect lung hyperinflation. Initial ventilatory setting were: oscillatory rate of 8.0 Hertz, inspiratory time 33% and bias flow of 15–20 l/min. Pressure amplitude (power) was adjusted as necessary to obtain adequate chest movement and $PaCO_2$ between 40 and 50 mmHg with pH above 7.30. If the pH was still lower than 7.30 and the $PaCO_2$ higher than 60 mmHg with a maximal power (10.0), the following interventions could be taken in consecutive order: i) bias flow could be increased to a maximum of 50 l/min; ii) oscillatory rate could be progressively decreased to a minimum of 3.0 Hertz; iii) inspiratory time could be increased to a maximum of 50%.

Measurements

Paw was measured at the airway proximal to the endotracheal tube with the manometer incorporated in both the Sensormedics oscillator and Siemens ventilator. All patients have an arterial catheter connected to a pressure transducer (Summit Model 33-260, Baxter Healthcare Corporation, Irvine, CA), hooked to a clinical cardiorespiratory monitor (Kontron Instruments, 7250, England). A pulmonary artery catheter (Edwards Swan-Ganz Thermodilution Catheter, Baxter Healthcare Corporation, Irvine, CA) had been previously introduced in all patients. Cardiac output was measured by thermodilution with the injection of 3 or 5 ml of ice cold saline. The average of 3 measurements was used for calculations. Standard formulas were used for calculations of other hemodynamic parameters.

Statistics

Wilcoxon signed rank test was used to compare values immediately before and after HFOV. Friedman repeated measures analysis of variance on ranks coupled with Dunn's method for multiple comparison of group versus control was used to assess changes during the 12 h before and 24 h after HFOV. Statistical significance was set at $p < 0.05$. All numbers and figures are expressed as median and range.

Results

Paw increased significantly with HFOV (median 20.9 cmH_2O, range 16.9–30.0 cmH_2O in CMV, versus median 30.0 cmH_2O, range 21.0–33.0 cmH_2O in HFOV, $p = 0.008$) (Table 2). Hyperinflation was not detected, nor was development or progression of ALS observed during this period. The alveolar-arterial oxygen difference decreased from 557.2 mmHg (range 360.4–607.8 mmHg) on CMV to 410.5 mmHg (range 282.9–500.2 mmHg) after 24 h of HFOV ($p = 0.03$) (Table 2). No statistically significant changes were observed in the oxygen index, although the median decreased from 44.0 (range 16.7–48.9) to 35.0 (range 23.9–54.7) after 24 h.

The heart rate tended to decrease, reaching statistical significance at 24 h (median of 162 bpm, range 129–178 bpm in CMV, versus median of 142 bpm, range 104–195 bpm after 24 h of HFOV, $p = 0.03$) (Table 2). No statistically significant changes were observed on mean systemic arterial pressure, central venous pressure, pulmonary artery occlusion pressure, mean pulmonary arterial pressure, systemic vascular resistance index, or pulmonary vascular resistance index. Cardiac index and oxygen delivery did not change significantly in the group as a whole (Table 2, Fig. 1), although in one individual a marked decrease was observed (Fig. 1). No changes in inotropic support were observed during the 24 h before and after initiation of HFOV. Two patients received fluid boluses to increase preload both in the 24 h period before and after HFOV (range of 10 to 20 ml/kg), although no evidence of decreased cardiac output was registered.

Discussion

We found that a high proximal Paw used during the initial period of HFOV was well tolerated by the cardiovascular system in all but one of our patients. No differences were found in oxygen delivery and cardiac index before and after HFOV. The statistical power for detecting a 25% reduction in oxygen delivery or cardiac index using a paired t-test procedure is 0.92 and 0.82, respectively ($\alpha = 0.05\%$). Smaller reductions may not be noted in this study, mainly because the small number of patients studied. Furthermore, it is worrisome that in one patient a clinically significant decrease in cardiac index and oxygen delivery was observed (Fig. 1). It is possible in this patient we did not recognize the moment when Paw needed to be decreased after alveolar re-expansion, and therefore a word of caution must be expressed.

Experimental evidence supports the initial use of high Paw during HFOV to obtain alveolar recruitment, followed by decreasing Paw when compliance improves due to alveolar reexpansion. The use of an optimal lung volume strategy is not an original idea in HFOV strategy [6]. Hamilton [7] and McCulloch [8] proved that HFOV can prevent ventilator induced lung injury if an adequate lung volume is maintained. Kinsella [9] showed that HFOV improved oxygenation when adequate pressure to expand the lung was used in premature baboons. A randomized multicenter trial (HIFI study group) [4] found that HFOV did not improve mortality or BPD incidence, and indeed the frequency of air leak, intraventricular hemorrhage, and periventricular leukomalacia was higher in the HFOV-treated group. An optimal lung volume strategy was not used in that study [10]. A second smaller randomized trial in premature newborns [5], using an opti-

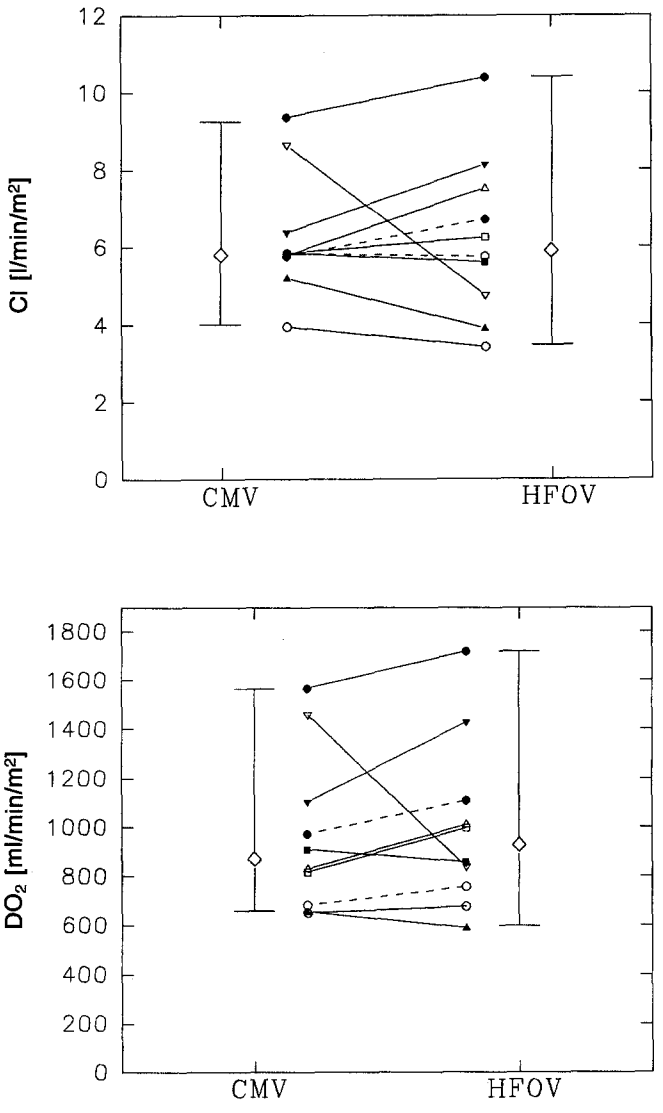

Fig. 1 Cardiac index (*upper panel*) and oxygen delivery index (*lower panel*) before and after high frequency oscillatory ventilation. Group values are expressed as median and range. Individual values plotted between group values. *Brackets lines* expressed individual values of patients placed on HFOV in a second period. *CI* Cardiac index; DO_2 Oxygen delivery index; *CMV* Conventional mechanical ventilation; *HFOV* High frequency oscillatory ventilation

mal lung volume strategy, found lower incidence of chronic lung injury in HFOV-treated babies, with no differences in mortality or in the incidence of pneumothorax and intraventricular hemorrhage.

The need for higher Paw in HFOV raised the concern about adverse effects in the cardiovascular system. Traverse [11–12] and Osiovich [13] showed impairment of cardiovascular function when Paw was increased in HFOV. These observations led them to speculate that the use of high mean airway pressures to achieve optimal lung volumes will be accompanied by deterioration of cardiovascular status. However, these studies evaluated acute changes in non-resuscitated models of acute lung injury, a model that cannot be extrapolated to the clinical setting, where the lung injury develops comparatively slowly, and where the subjects will receive volume resuscitation to maintain preload. A high volume/pressure strategy was not used in either of these studies. The work of Kinsella [9] showed that in premature baboons ventilated with HFOV no deleterious cardiovascular effects were observed. The strategy in this study consisted of the use of enough pressure to obtain adequate oxygenation, but reducing pressures when changes in lung inflation (compliance) and improvements in oxygenation were observed.

In 1985, Vincent observed no hemodynamic effects on cardiac post-operative patients ventilated with low Paw HFOV [14]. Both strategy (low Paw) and population (non ARDS patients) are completely different compared to the present study. Arnold [15] recently presented the first report of the use of HFOV in non neonatal pediatric patients with severe respiratory failure. In his series, high lung volume strategy was used to obtain alveolar re-expansion. Six of the 7 patients responded to HFOV with that approach. Hemodynamic data of 4 of those patients showed no compromise of cardiovascular function despite the use of high Paw. A high preload was maintained to achieve hemodynamic stability.

It is unclear how much pressure is actually transmitted to intrathoracic organs by lungs with decreased compliance. Traverse [11–12] illustrated this problem demonstrating less cardiovascular effects of the airway pressure when lung compliance was acutely decreased by bronchoalveolar lavage in cats. It is also unclear how comparable the Paw measured during CMV is with the Paw measured during HFOV. Gerstmann et al. [16] showed in normal rabbits ventilated with HFOV that tracheal pressure is always lower than proximal airway pressure, while alveolar pressure can be lower than, equal to, or higher than proximal pressure depending on the site of measurement (superior versus middle lobe). Other reports confirm the inhomogeneity of mean alveolar pressure while on HFOV [17–20].

The modest decrease in heart rate at the end of the study period may be caused by the improvement in oxygenation. It is unlikely that this change reflect any effect of HFOV itself.

We conclude that high initial Paw during HFOV must be used cautiously, but in most patients no deleterious hemodynamic effects are observed.

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Table 2 Respiratory and hemodynamic variables before and after high-frequency oscillatory ventilation

	CMV[a]	HFOV[b]			
		1 h	6 h	12 h	24 h
Paw[c] (cmH_2O)	20.9 (16.9 – 30.0)	30.0 (21.0 – 33.0)	29.0 (24.0 – 44.0)°	30.0 (23.0 – 43.0)	30.5 (23.0 – 39.0)
$P(A\text{-}a)O_2$[d] (mmHg)	557.2 (360.4 – 607.8)	525.2 (291.3 – 602.8)	520.2 (277.6 – 608.5)	421.6 (306.0 – 582.7)	410.5 (282.9 – 500.2)
PaO_2/FIO_2	62.2 (43.0 – 104.6)	87.8 (40.0 – 115.0)	83.5 (57.0 – 165.0)	82.3 (53.2 – 121.7)	83.2 (65.0 – 116.7)
OI[e]	44.0 (16.7 – 48.9)	32.7 (23.5 – 82.5)	36.8 (15.8 – 79.0)	40.1 (15.8 – 65.6)	35.0 (23.9 – 54.7)
$PaCO_2$ (mmHg)	45 (36 – 58)	58 (32 – 77)	42 (38 – 78)	40 (25 – 55)	40 (28 – 51)
HR[f] (bpm)	162 (129 – 178)	160 (132 – 174)	154 (124 – 182)	147 (114 – 182)	142 (104 – 195)°
MAP[g] (mmHg)	74 (60 – 136)	78 (65 – 85)	79 (67 – 96)	79 (66 – 111)	82 (59 – 111)
CVP[h] (cmH_2O)	10 (7 – 24)	11 (5 – 22)	14 (5 – 22)	12 (7 – 20)	12 (6 – 20)
PAOP[i] (cmH_2O)	12 (8 – 17)	16 (10 – 23)	15 (10 – 23)	15 (10 – 22)	16 (7 – 23)
MPAP[j] (cmH_2O)	32 (28 – 42)	37 (21 – 41)	36 (23 – 39)	36 (24 – 43)	36 (26 – 40)
CI[k] ($l/min/m^2$)	5.8 (4.0 – 9.4)	5.9 (3.4 – 10.4)	5.6 (3.9 – 6.8)	5.3 (3.9 – 8.5)	4.5 (3.5 – 6.1)
DO_2[l] ($l/min/m^2$)	870.7 (650.9 – 1566.3)	927.8 (590.0 – 1720.2)	871.4 (590.0 – 1100.9)	801.7 (577.4 – 1273.8)	751.3 (588.9 – 941.4)
PVRI[m] ($dyne \cdot s/cm^5 \cdot m^2$)	322.3 (200.9 – 603.8)	280.4 (117.0 – 584.6)	288.2 (142.2 – 354.7)	290.8 (132.0 – 357.0)	336.8 (253.0 – 395.3)
SVRI[n] ($dyne \cdot s/cm^5 \cdot m^2$)	949.6 (490.8 – 2614.4)	923.4 (599.4 – 1800.6)	973.4 (665.4 – 1503.1)	1101.4 (509.0 – 1503.1)	1183.4 (722.4 – 1803.7)

Values are expressed as median and range
[a] *CMV* conventional mechanical ventilation
[b] *HFOV* high-frequency oscillatory ventilation
[c] *Paw* mean airway pressure
[d] *P(A-a)O₂* alveolar-arterial oxygen difference
[e] *OI* oxygen index
[f] *HR* heart rate
[g] *MAP* mean arterial blood pressure
[h] *CVP* central venous pressure
[i] *PAOP* pulmonary artery occlusion pressure
[j] *MPAP* mean pulmonary artery pressure
[k] *CI* cardiac index
[l] *DO₂* oxygen delivery
[m] *PVRI* pulmonary vascular resistance index
[n] *SVRI* systemic vascular resistance index
° $p<0.05$

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