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High frequency oscillatory ventilation for respiratory failure due to RSV bronchiolitis

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Conclusion: RSV induced respiratory failure with hypercapnia can be managed with HFOV using high mean airway pressure and large pressure swings while preserving spontaneous breathing.

Keywords: Respiratory syncytial virus · High frequency oscillatory ventilation · Bronchiolitis · Respiratory failure · Hypercapnia

Introduction

Despite the use of non invasive respiratory support such as CPAP [1, 2], helium–oxygen mixture [3], alone or in combination [4], the proportion of infants with RSV infection requiring conventional mechanical ventilation (CMV) is still reported to vary around 25% in those requiring intensive care admission [1, 5]. Adequate CMV in obstructive lung disease represents a challenge. High tidal volumes and minute ventilation are required implying high peak pressures, risk of air leaks, and an almost universal use of muscular paralysis [6]. The use of high frequency oscillatory ventilation (HFOV) has been described in a few cases [7–10] as a rescue intervention to improve severe hypoxemic respiratory failure while CO2 elimination was yet achieved. In this report, we aim to
describe the time course of HFOV in RSV proven infection with predominantly hypercapnic respiratory failure as an effective alternative to conventional mechanical respiratory support.

**Methods**

Charts of all infants with confirmed RSV bronchiolitis treated with high frequency oscillatory ventilation between 01.01.1998 and 01.01.2007 were reviewed. Those with a known underlying condition susceptible to modify the nature or the course of the lung disease such as broncho-pulmonary dysplasia, pulmonary congenital malformation or non operated congenital heart disease were excluded. The obstructive pattern of the lung disease for 6 infants initially on CMV, was determined according to the relation between mean airway pressure and the alveolo–arterial oxygen pressure difference (AaDO2) described by Tasker et al. [11] and lung expansion was assessed for each infant by counting the total number of visible ribs (on both hemithoraces) above the diaphragm on the initial chest X-ray as described by Greenough et al. [12], 16 ribs being the cut-off value for the presence of lung overexpansion.

During the course of mechanical ventilation, no pharmacological treatment such as corticosteroids, β2 or α-adrenegic agonists were administered. Bacterial co-infection was suspected on clinical deterioration and antibiotics given if gram staining of tracheal secretions, blood leucocytes count, differential and serum CRP were considered abnormal.

CMV was delivered with a Babylog 8000 (Dräger, Lubeck, Germany) in a pressure controlled mode and HFOV through an electromagnetically driven membrane oscillator (3100 A Sensor Medics Critical Care, Yorba Linda, CA, USA). Frequency was started between 8–12 Hz with an I:E ratio of 0.33 and mean airway (meanaw) pressure 2 cmH2O above the last value set during conventional ventilation. It was raised by steps of 2 cmH2O aiming at an arterial saturation above 88% until a reduction in FiO2 could be initiated. Additional recruitment manoeuvres were not attempted. Peak to peak pressure amplitude was started at a value where chest movements could be visually detected and stepwise increased to reach and maintain the pH above 7.25 irrespective of the PaCO2. Infants received midazolam or chloral hydrate for sedation and morphine sulphate for analgesia. Muscular paralysis was avoided as long as not specifically required.

Ventilatory settings (FiO2, meanaw pressure, peak to peak amplitude, ventilatory frequency, I:E ratio), blood gases and vital signs (infants respiratory rate, mean arterial blood pressure and heart rate) were extracted during conventional mechanical ventilation (period CMV), a mean of 3 h (±40 min) after the switch to HFOV (period HFOVi), mid course (period HFOVm), just prior stopping HFOV (period HFOVe) and after extubation either on CPAP and/or supplemental oxygen therapy (Post-Extub).

**Statistics**

Kruskall–Wallis non parametric analysis of variance was performed to compare periods of respiratory support for ventilatory variables, gas exchanges and vital signs using a PRISM 4.0 package (GraphPad software). P < 0.05 was considered significant.

**Results**

A total of 13 infants with RSV proven lung infection were treated with HFOV during the study period. Four cases were excluded from analysis (two with congenital pulmonary malformation, two with unrepaired congenital cardiac disease). Three infants, transferred after intubation from another unit or hospital were treated with HFOV as first intention. Six infants, intubated in our ICU, were put on HFOV after a median (25–75%) period of CMV of 3.5 (1–32.5) h. The relevant demographic data, initial lung pattern and clinical course are described in Table 1. All infants attested of lung overexpansion on chest X-ray [12] while none fulfilled the criteria for an ARDS type of RSV infection [11]. Bacterial co-infection was diagnosed in five infants (56%). Before initiating HFOV in the six cases under CMV, mean (SD) pH was 7.27 (0.15) units and PaCO2 72 (22) mmHg with a mean peak inspiratory pressure of 26 (5) cmH2O and a PEEP of 6.5 (1) cmH2O. Changes in ventilatory settings, blood gases, infants own respiratory rates, heart rates and mean arterial pressures, doses of medication given during the various periods of ventilation are summarized in Table 2. No infant was paralyzed. Hemodynamically, two infants were treated with dopamine. One infant had developed a bilateral pneumothorax under CMV which resolved with drainage and HFOV. Five infants were extubated to CPAP, the other to simple supplemental oxygen and all survived.

**Discussion**

Although mechanical ventilation at high frequencies is usually considered to be contraindicated in lung disease with increased airway resistance, the successful use of
rescue HFOV in a few infants with bronchiolitis to correct severe hypoxemia [7–9] or in a case of status asthmaticus [14] has yet been published. Our report documents that HFOV can be used as an elective alternative to CMV to support spontaneous respiration and improve gas exchanges in infants with predominantly obstructive and hypercapnic respiratory failure from small airway disease. Indeed, despite bacterial co-infection in half of them, either by scoring the chest X-ray [12] or plotting the individual alveolo–arterial oxygen difference against meanaw pressure [11], all infants showed a predominantly overexpanded lung pattern [15].

In our view, the use of HFOV in bronchiolitis demonstrates several advantages over CMV. It obviates the need for infant ventilator synchrony and allows muscular paralysis to be avoided. PaCO2 can be controlled by adjusting peak to peak pressure while the infant continues actively to contribute to expiration under usual sedation. We consistently observed that the infant’s respiratory rate slowly increased as pressure amplitudes were decreased (see Fig. 1). A bilateral pneumothorax observed under CMV resolved during HFOV and no new air-leak occurred but the number of infants is too small to draw conclusions. Hemodynamically, a few infants did require adrenergic support but renal function was well preserved as suggested by the physiological metabolic compensation of the respiratory acidosis that occurred over time. The mean duration of HFOV was either similar [11, 16] or slightly shorter to that reported in infants with obstructive bronchiolitis using CMV [6, 15] and all patients could be extubated directly to CPAP or supplemental Oxygen.

The major limitation of this report is its retrospective and descriptive nature. HFOV settings were set on pragmatic grounds because the actual knowledge on mechanisms governing pressure and flow transmission when peripheral airway resistance is high, is scarce [17].

### Table 1: Demographic and initial clinical data of the nine infants, six with prior CMV

| No. | Age at entry (days) | Weight (g) | Aa–DO2 (mmHg) | Mean airway pressure (cmH2O) | Number of ribs visible | HFOV length (h) | Bacterial co-infection |
|-----|---------------------|------------|---------------|-----------------------------|------------------------|----------------|------------------------|
| 1   | 28                  | 4,000      | –             | –                           | 19                     | 94             |                        |
| 2   | 36                  | 3,600      | –             | –                           | 16                     | 120            |                        |
| 3   | 80                  | 2,900      | 326           | 14                          | 19                     | 135            | *K. Pneumoniae*        |
| 4   | 112                 | 5,800      | 125           | 14                          | 18                     | 192            | *H. Influenzae*        |
| 5   | 35                  | 2,300      | 289           | 14                          | 22                     | 104            |                        |
| 6   | 32                  | 3,055      | 342           | 12                          | 20                     | 60             | *H. Influenzae*        |
| 7   | 49                  | 3,700      | 376           | 10                          | 17                     | 139            | *S. Pneumoniae*        |
| 8   | 114                 | 2,900      | 236           | 11                          | 17                     | 147            | *S. Pneumoniae*        |
| 9   | 19                  | 4,000      | –             | –                           | 20                     | 93             | *H. Influenzae*        |
| Mean (SD) | 56 (34) | 3,585 (950) | 282 (25) | 12.5 (2) | 18.7 (1.8) | 120 (38) |

a Number of visible ribs above the diaphragms on both lung fields: significant lung overexpansion is recognized above 16 ribs [12]

### Table 2: Mean (SD) of ventilatory settings, blood gases, infants respiratory rate and dosage of sedatives and analgesics through the different periods of respiratory support

|                | CMV (n = 6) | HFOi (n = 9) | HFOm (n = 9) | HFOe (n = 9) | Post-Extub (n = 9) |
|----------------|-------------|--------------|--------------|--------------|-------------------|
| Mean airway pressure (cmH2O) | 12.5 (2)    | 18.9* (2.7)  | 14.5 (3.3)   | 11.1** (1.3)  |                   |
| Peak to peak pressure (cmH2O)  | 44.9 (12.4) | 39.3 (11)    | 10.9 (1.5)   | 21.1** (7.7)  |                   |
| HFOV Frequency (Hz)            | 11.1 (1.9)  | 10.9 (1.5)   | 10.4 (2.0)   | 10.4 (2.0)    |                   |
| FiO2 (%)                      | 0.68 (0.18) | 0.59 (0.14)  | 0.36 (0.8)   | 0.29** (0.6)  | 0.26 (0.5)       |
| pH                           | 7.27 (0.15) | 7.33 (0.08)  | 7.37 (0.04)  | 7.42** (0.03) | 7.40 (0.03)      |
| PaCO2 (mmHg)                  | 72 (22)     | 56 (10)      | 54 (9)       | 47 (8)        | 51 (7)           |
| Base excess                   | 3.5 (4)     | 3.2 (5)      | 5.5 (3.3)    | 7.0 (2.6)     | 6.1 (2.4)        |
| Respiratory rate (breaths/min) | 61 (20)     | 20* (11)     | 34 (19)      | 34 (14)       | 41 (11)          |
| Heart rate (beats/min)        | 168 (19)    | 156 (16)     | 137 (16)     | 140 (26)      | 136 (20)         |
| Mean arterial pressure (mmHg) | 49 (19)     | 52 (11)      | 52 (9)       | 49 (7)        | 62 (10)          |
| Mean midazolam (µg/kg/h) (SD) | 110 (66)    | 113 (64)     | 106 (69)     |               |                   |
| Mean morphine (µg/kg/h) (SD)  | 25 (18)     | 14 (12)      | 14 (12)      | 14 (12)       |                   |

CMV Conventional mechanical ventilation, HFOVi initial period of high frequency oscillatory ventilation, HFOVm middle period during high frequency oscillatory ventilation, HFOVe end period of high frequency oscillatory ventilation. *P < 0.05 CMV vs HFOVi. **P < 0.05 HFOVi vs HFOVe
In this view, three settings deserve comments: the large peak to peak pressure, the low ventilatory frequency and the high mean\textsubscript{aw} pressure compared to HFOV in idiopathic respiratory distress syndrome [18]. Such settings seem at first poorly adapted to the ventilation of obstructive lung disease. However, with HFOV, the transmission of pressures and volumes delivered by the ventilator is exquisitely sensitive to the mechanical properties of the respiratory system and the endotracheal tube [19]. Thus, the requirement of high peak to peak pressure can be explained by the dampening that occur through the small endotracheal tube and down the highly resistive airway of these infants, reducing pressure swings and effective tidal volume [19, 20]. A low frequency can thus be advocated to maintain an adequate tidal volume once high amplitude has been set.

The high mean\textsubscript{aw} pressure required at the airway opening is a hallmark of all cases reported with HFOV in small airway disease [9, 10, 13] and represents the most intriguing setting. It is partly attributed to the pressure drop occurring through the flow dependant resistance of the endotracheal tube which is accentuated when using an I:E of 0.33 generating higher inspiratory than expiratory flows [19]. More importantly, this high mean\textsubscript{aw} pressure is considered necessary to generate a sufficient pressure to open and stent the collapsed small airway, allowing pressure swings to be transmitted peripherally and alveolar ventilation to resume in obstructed lung units. In this concept termed the “open airway” concept, mean\textsubscript{aw} pressure becomes a major determinant of CO\textsubscript{2} elimination [9, 10, 13, 14]. The optimal pressure required to open the peripheral airway without causing alveolar overdistention and adverse cardiovascular effects must lie in a narrow range. It still requires an experimental set- up to be approximated scientifically [20].

In conclusion, HFOV seems a valuable tool to support spontaneous respiration and gas exchange in infants with respiratory failure due to the common obstructive lung pattern of RSV infection. Determination of optimal ventilatory settings remains a difficult clinical task due to the complexity of the interaction between mean\textsubscript{aw} pressure, frequency, pressure amplitude and mechanical characteristics of the respiratory system.

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