The Journal of Maternal–Fetal and Neonatal Medicine 2003;13:398–402

Use of high-frequency jet ventilation in neonates with hypoxemia refractory to high-frequency oscillatory ventilation

P. Friedlich, N. Subramanian, M. Sebald, S. Noori and I. Seri

USC Division of Neonatal Medicine, Childrens Hospital Los Angeles and the Women's and Children's Hospital, LAC+USC Medical Center; Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, California, USA

Objective: To describe the response to high-frequency jet ventilation in infants with hypoxemic respiratory failure unresponsive to high-frequency oscillatory ventilation.

Methods: This was a retrospective analysis of chart records on demographics, ventilator settings, blood gas analysis and calculated oxygenation index prior to and during the first 7 days of high-frequency jet ventilation in ten consecutive infants.

Results: Before the initiation of high-frequency jet ventilation, the ventilatory mean airway pressure (MAP; cmH_2O), fraction of inspired oxygen (FiO_2) and oxygenation index on high-frequency oscillatory ventilation were 14.3 ± 1.3, 0.97 ± 0.02 and 29 ± 5, respectively. Three hours after the initiation of high-frequency jet ventilation, the oxygenation index improved to 18 ± 4 ($p < 0.001$) and the improvement was sustained during the study period. By 6 h of high-frequency jet ventilation, the FiO_2 decreased to 0.62 ± 0.09 ($p < 0.01$) and, by 1–3 h of ventilation, the MAP decreased to 10.9 ± 1.3 ($p < 0.01$). The improvement in FiO_2 persisted for 7 days while, although the MAP remained lower throughout the study, the improvement in MAP failed to reach statistical significance after 72 h. No significant changes in pH, pCO_2, or pO_2 before or during high-frequency jet ventilation were noted.

Conclusion: High-frequency jet ventilation improves hypoxemic respiratory failure unresponsive to high-frequency oscillatory ventilation in infants. These findings suggest that not all high-frequency ventilatory devices yield the same clinical results.

Key words: HIGH-FREQUENCY JET VENTILATION; HIGH-FREQUENCY OSCILLATORY VENTILATION; HYPOXEMIC INFANTS; RESPIRATORY FAILURE

INTRODUCTION

Progress in our understanding of the pathophysiology and the treatment of neonatal respiratory failure represents one of the major recent advances in neonatology[1,2]. The availability of novel modalities of mechanical ventilation ranging from different modes of advanced conventional ventilation to high-frequency ventilation has directly contributed to improvements in the care of the critically ill neonate and infant[3–8]. In the presence of poorly compliant lungs, high ventilatory pressures associated with classical conventional ventilation involving high tidal volume often lead to baro- and volutrauma and the development of air leak syndromes. The advent of high-frequency ventilation has allowed the use of higher mean airway pressures (MAP) without high peak inspiratory pressures (PIP). Thus, high-frequency ventilation attenuates the large pressure and volume changes associated with conventional ventilation, therefore resulting in a decrease in the incidence and severity of lung injury[7–14].

Classical complications of high-tidal-volume conventional mechanical ventilation include the development of chronic lung disease and the ensuing need for long-term mechanical ventilatory support. Preterm neonates with chronic lung disease often develop acute respiratory decompensation, most frequently as a consequence of recurrent infections. The lung mechanics of these infants are characterized by a further decrease in compliance and an increase in airway resistance. These patients are often

Correspondence: Dr P. Friedlich, Childrens Hospital Los Angeles, 4650 Sunset Blvd MS no. 31, Los Angeles, CA 90027, USA

Received 15–03–03 Accepted 03–04–03

treated with high-frequency oscillatory ventilation and many of them may respond to this treatment modality.

However, owing to the development of the vicious cycle of gas trapping and lung over-inflation, preterm neonates with chronic lung disease and significantly increased airway resistance and low compliance may not always respond to high-frequency oscillatory ventilation. Under these clinical circumstances, lengthening the expiratory time by decreasing the inspiratory to expiratory time ratio (I : E ratio) may improve gas exchange. However, the lowest I : E ratio that can be achieved on high-frequency oscillatory ventilation is 1 : 2. Furthermore, the active exhalation phase of the high-frequency oscillatory ventilation device may promote airway collapse in preterm neonates when lower airway pressures are used in an effort to avoid lung over-inflation. Therefore, the use of a low-volume ventilatory strategy with high-frequency oscillatory ventilation may further exacerbate the hypoxemic status in the preterm neonate with chronic lung disease and hypoxic respiratory failure due to gas trapping. Since the I : E ratio is in the 1 : 3.5 to 1 : 11.5 range on high-frequency jet ventilation, and since the exhalation phase is passive when this ventilation modality is used, we treated preterm neonates with chronic lung disease and hypoxemic respiratory failure unresponsive to high-frequency oscillatory ventilation with high-frequency jet ventilation. In this report, we present our experience in ten preterm neonates with chronic lung disease who remained hypoxemic despite the use of high-frequency oscillatory ventilation.

METHODS

Patient selection criteria and indication for the use of high-frequency jet ventilation

Preterm neonates with chronic lung disease requiring mechanical ventilation for at least 4 weeks and transferred to the neonatal intensive care unit (NICU) of the Childrens Hospital Los Angeles (CHLA) for hypoxemic respiratory failure were initially managed with 3001A Sensormedics high-frequency oscillatory ventilation (Sensormedics Inc., Yorba Linda, CA, USA). Ten critically ill neonates from this group of patients could not be adequately oxygenated with high-frequency oscillatory ventilation, despite multiple changes in MAP and oscillatory frequencies, probably as a consequence of gas trapping and their severe lung disease. In an attempt to resolve the hypoxemic respiratory failure, these patients were placed on high-frequency jet ventilation and their data were retrospectively collected; the findings are presented in this paper. None of these patients received steroid treatment during the first 72 h of high-frequency jet ventilation.

For the purposes of this study, chronic lung disease is defined as at least a 4-week requirement for mechanical ventilation in the presence of characteristic radiological changes in preterm neonates. Pneumonia was defined by characteristic X-ray findings and/or laboratory and bacteriological findings on bronchoalveolar lavage and blood samples. Respiratory failure was defined as an oxygenation index of > 20 with the use of a MAP providing optimum lung expansion on high-frequency oscillatory ventilation. Optimum lung expansion was considered to have been achieved on high-frequency oscillatory ventilation if the base of the right lung was between the 9th and 10th ribs in the right mid-clavicular line.

Ventilators and ventilator strategies

The 3001A Sensormedics high-frequency oscillatory ventilator and the Life Pulse High-Frequency Jet ventilator (Bunnell Inc., Salt Lake City, UT, USA) were used for high-frequency ventilation in this study. For the use of the high-frequency jet ventilator an endotracheal tube adaptor (LifePort™, Bunnell Inc., Salt Lake City, UT, USA) of appropriate size was utilized. The high-frequency jet ventilator senses airway pressure near the tip of the endotracheal tube. A conventional ventilator (Newport Breeze, Newport Beach, CA, USA) was the source of bias flow of heated, humidified gas, at the same fraction of inspired oxygen ($F\text{iO}_2$) as the jet ventilator. The conventional ventilator generated the positive end-expiratory pressure (PEEP) and provided intermittent sigh breaths in the form of background intermittent mandatory ventilation.

In all patients, the high-frequency jet ventilator was initially set at 420 cycles/min with an inspiratory time of 0.02 s. The $F\text{iO}_2$ was set to achieve O_2 saturation between 88% and 95%. The PEEP was initially set at 5–7 cmH_2O and adjusted according to the level of oxygenation and the need for alveolar recruitment, monitored by serial chest X-rays and arterial blood gas findings. The PIP of the high-frequency jet ventilator was set to achieve a delta pressure (ΔP) to keep the arterial partial pressure of CO_2 ($P\text{aCO}_2$) between 45 and 55 mmHg. Background intermittent mandatory ventilation was set between 3 and 5 breaths/min with an inspiratory time of 0.35 s. Appropriate oxygenation was achieved by making changes in $F\text{iO}_2$ and MAP, while ventilation was controlled by adjusting the tidal volume (PIP – PEEP) and by manipulation of jet frequency.

The patients were continuously monitored for changes in transcutaneous O_2 and CO_2 tension and O_2 saturation. Arterial blood gases were obtained within the first 3 h, at 6–12 h, at 24 h and later daily, or as clinically indicated. The oxygenation index was calculated using the formula: oxygenation index = (mean airway pressure $\times$ $F\text{iO}_2$)/$P\text{aO}_2$.

For the purposes of this study, an oxygenation index of > 20 was considered as evidence of hypoxic respiratory failure.

Data collection and statistics

Demographics and ventilatory settings on high-frequency oscillatory ventilation and during high-frequency jet ventilation were collected. Lengths of the use of the high-frequency jet ventilation were recorded. Statistical analysis was performed using the GB-STAT™ version 7.0 (Dynamic Microsystem Inc., Silver Spring, MD, USA). Continuous variables were analyzed by *t* test and analysis of variance for repeated measures. Data are presented as mean ± standard deviation (SD). A p value of < 0.05 was considered significant.

RESULTS

Patient characteristics and ventilator settings on high-frequency oscillatory ventilation prior to the initiation of high-frequency jet ventilation are given in Table 1, while the response to high-frequency jet ventilation in the oxygenation index, FiO_2 and MAP are presented in Figure 1.

With the exception of patient 1, who died from circulatory collapse from septic shock within 3 h of the initiation of high-frequency jet ventilation, the other neonates presented with chronic lung disease and pneumonia. It is conceivable that the new-onset pulmonary infection resulted in the development of the hypoxic respiratory failure in this patient population with the underlying chronic lung changes.

The oxygenation index decreased from a baseline mean of 29 ± 5 to 18 ± 4 ($p < 0.001$) at 3 h of high-frequency jet ventilation. This statistically significant decrease was sustained throughout the study (Figure 1a). FiO_2 requirements decreased from 0.97 ± 0.02 to 0.62 ± 0.09 by 6 h of high-frequency jet ventilation ($p < 0.01$) and remained statistically lower throughout the use of high-frequency jet ventilation (Figure 1b). MAP decreased from 14.3 ± 1.3 to 10.9 ± 1.3 cmH_2O after 1–3 h of high-frequency jet ventilation ($p < 0.01$) and remained lower throughout the study. However, the difference in the MAP between the high-frequency oscillatory ventilation and high-frequency jet ventilation remained statistically significant for 72 h of high-frequency jet ventilation only (Figure 1c) and, although the MAP was lower by more than 20% by the end of the study period (7 days), this difference did not reach statistical significance. No changes in the pH, PaO_2, and $PaCO_2$ occurred during the study (Figure 2).

The mean length of high-frequency jet ventilation was 172 h. No ventilatory complications were noted during the use of high-frequency jet ventilation, including air leak syndrome, and no changes in inotropic support occurred during high-frequency jet ventilation. One patient (patient 6) with *Pseudomonas aeruginosa* pneumonia could not be adequately ventilated on high-frequency jet ventilation and was placed on synchronized intermittent mandatory ventilation with pressure support after 1 h of high-frequency jet ventilation. The overall survival rate to discharge was 90%, with one patient (patient 1) expiring within the first 3 h of high-frequency jet ventilation from septic shock. The survivors all had an oxygen requirement at the time of discharge, indicating the severity of their pulmonary disease resulting in the development of hypoxic respiratory failure.

Table 1 Patient characteristics and ventilator settings on high-frequency oscillatory ventilation prior to the initiation of high-frequency jet ventilation (HFJV)

Patient	GA (weeks)	PNA (days)	Diagnosis	MAP (cmH_2O)	FiO_2	Frequency (Hz)
1	28	41	CLD/sepsis	17.0 (13–18)	1	7 (6–10)
2	28	29	CLD/pneumonia	16.5 (12–17)	1	6 (5–8)
3	23	33	CLD/pneumonia	15.0 (14–16)	1	7 (6–10)
4	26	115	CLD/pneumonia	13.0 (11–14)	1	6 (6–10)
5	28	29	CLD/pneumonia	21.0 (16–22)	1	5 (5–7)
6	24	31	CLD/pneumonia	12.0 (10–13)	1	7 (6–10)
7	23	28	CLD/pneumonia	11.0 (11–14)	1	6 (6–10)
8	25	65	CLD/pneumonia	14.0 (9–17)	1	6 (5–8)
9	27	87	CLD/pneumonia	15.0 (11–18)	1	5 (5–7)
10	25	54	CLD/pneumonia	10.0 (10–14)	1	7 (7–10)

GA, gestational age; PNA, postnatal age at time of HFJV; MAP, mean airway pressure; FiO_2, fraction of inspired oxygen; CLD, chronic lung disease

Ranges are given in parentheses

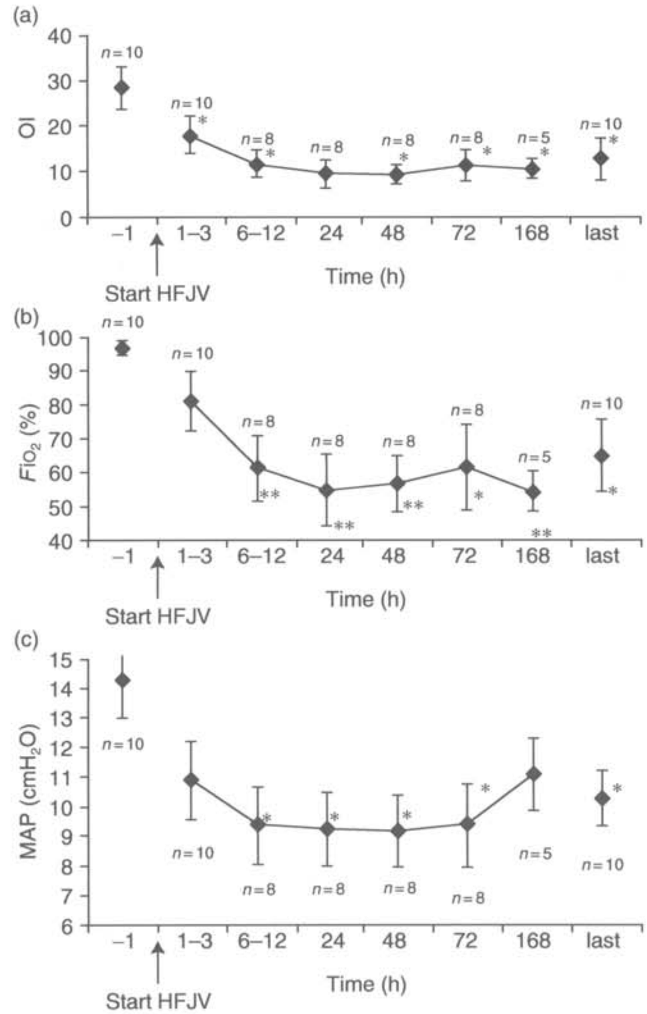

Figure 1 Changes in oxygenation index (OI)(a), fraction of inspired oxygen (FiO_2)(b) and mean airway pressure (MAP) (c) an hour prior to the initiation of high-frequency jet ventilation (HFJV) therapy, for the first week following treatment and last value prior to discontinuation of HFJV. Vertical bars indicate SD. p Values compare data following initiation of HFJV to pre-HFJV support: (a) $^*p < 0.001$; (b) $^*p < 0.05$, $^{**}p < 0.01$; (c) $^*p < 0.01$

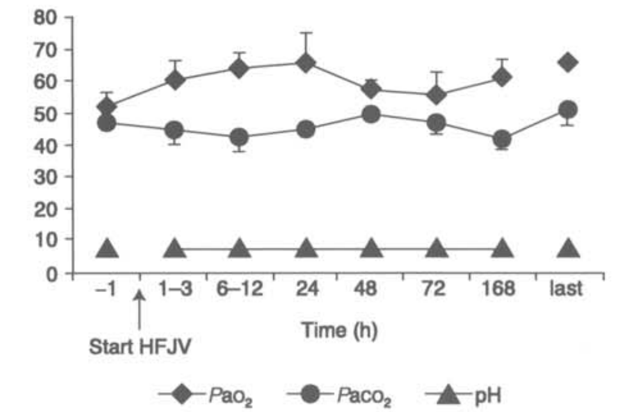

Figure 2 Changes in PaO_2, $PaCO_2$ and pH an hour prior to the initiation of high-frequency jet ventilation (HFJV) therapy, for the first week following treatment and last value prior to discontinuation of HFJV. Vertical bars indicate SD

DISCUSSION

The findings of this retrospective study suggest that the majority of preterm neonates with chronic lung disease and refractory hypoxemic respiratory failure unresponsive to high-frequency oscillatory ventilation and/or conventional mechanical ventilation can be adequately oxygenated and ventilated with high-frequency jet ventilation as indicated by the significant improvements in FiO_2, MAP and oxygenation index, and the 90% survival rate of this critically ill patient population with an expected mortality much higher than 10%.

Among the fundamental differences between high-frequency jet ventilation and high-frequency oscillatory ventilation are the lower I : E ratio and the longer passive exhalation phase on high-frequency jet ventilation. These differences may have significant implications in patients with lung conditions prone to developing gas trapping and lung over-inflation. During conventional mechanical ventilation, gas trapping can be minimized by allowing enough time during expiration for alveolar pressure to equilibrate with upper airway pressure, a concept known as the time constant. In addition, in the neonate, expiratory airway resistance is commonly at least four-fold greater than the inspiratory airway resistance. Therefore, to minimize the risks of gas trapping during conventional mechanical ventilation, the use of an I : E ratio of less than 1 : 2 is advocated. The lowest achievable I : E ratio on high-frequency oscillatory ventilation is 1 : 2, while it is in the 1 : 3.5 to 1 : 11.5 range on high-frequency jet ventilation. This property of the high-frequency jet ventilation significantly contributes to its ability to minimize gas trapping while maintaining lower lung volumes in preterm neonates with chronic lung disease and over-inflation.

Although, in theory, the exhalation phase is active on high-frequency oscillatory ventilation, the benefits are lost when mid- to lower-level bronchi have immature and/or disrupted architecture and thus more easily collapse during the active exhalation phase. This may be one of the mechanisms by which high-frequency oscillatory ventilation leads to air trapping when low-volume-strategy high-frequency oscillatory ventilation is attempted in critically ill preterm neonates with hypoxic respiratory failure. However, the extent to which gas trapping occurs during high-frequency oscillatory ventilation and the relationship between gas trapping and the high- versus low-volume strategy in the preterm infant need further clarification.

In the present study, despite attempts on high-frequency oscillatory ventilation to lower the oscillatory frequency to 5–7 Hz and manipulation of MAP to achieve optimum lung expansion, gas trapping and over-inflation could not be diminished. The marked improvement in the oxygenation index without a compromise in pH and pCO_2 in the preterm neonates with chronic lung disease and hypoxic respiratory failure on high-frequency jet ventilation in the present study may be explained, as stated earlier, by the passive and relatively longer exhalation phase of the jet, resulting in a decrease in gas trapping.

In conclusion, the findings of the present study suggest that high-frequency jet ventilation may have advantageous mechanical properties compared to those of high-frequency oscillatory ventilation that are important in the ventilatory management of critically ill preterm neonates with chronic lung disease, poor lung compliance, gas trapping and resultant hypoxic respiratory failure. These observations are also important in emphasizing that not all high-frequency ventilatory devices yield the same clinical results in the critically ill preterm neonate with immature and diseased airways and lung parenchyma.

REFERENCES

1. Mariani GL, Carla WA. Ventilatory management in neonates: science or art? *Clin Perinatol* 1998;25:33–48
2. Spitzer AB, Fox WW. Positive pressure ventilation: pressure-limited and time cycle ventilators. In Goldsmith JP, Karotin EH, eds. *Assisted Ventilation of the Neonates*, 3rd edn. Philadelphia, PA: WB Saunders, 1996:167–86
3. Carlo WA, Chatburn RL, Martin RJ. Decrease in airway pressure during high-frequency jet ventilation in infants with respiratory distress syndrome. *J Pediatr* 1984;1104:101
4. Spitzer AR, Buttler S, Fox WW. The ventilatory response to combined high frequency jet ventilation and conventional mechanical ventilation for the rescue treatment of severe neonatal lung disease. *Pediatr Pulmonol* 1989;7:244–9
5. Bunnell JB. High frequency ventilation of infants. In Rath M, ed. *Current Perinatology*. New York: Spinger-Verlag, 1990: 172–200
6. Clark RH, Gerstmann DR, Null DM, *et al.* Prospective randomized comparison of high frequency oscillatory and conventional ventilation for respiratory distress syndrome. *Pediatrics* 1992;89:5–12
7. Gerstmann DR, Minton SD, Stoddart RA, *et al.* The provo multicenter early high frequency oscillatory ventilation trial: improved pulmonary and clinical outcome in respiratory distress syndrome. *Pediatrics* 1996;98:1044–52
8. Schultze A, Gerhardt T, Musante G, *et al.* Proportional assist ventilation in low birth weight infants with acute respiratory disease: a comparison to assist/control and conventional mechanical ventilation. *J Pediatr* 1999;135:339–44
9. Simon BA, Weinmann GG, Mitzner W. Mean airway pressure and alveolar pressure during high frequency ventilation. *J Appl Physiol* 1984;57:1069–78
10. Solway J, Rossing TH, Saari AF, *et al.* Expiratory flow limitation and dynamic pulmonary hyperinflation during high frequency ventilation. *J Appl Physiol* 1986;60:2071–8
11. Smith DW, Frankel LR, Ariagno RL. Dissociation of mean airway pressure and lung volume during high frequency oscillatory ventilation. *Crit Care Med* 1988;16:531–5
12. Bunnell JB. General concepts of high frequency ventilation. In Donn SM, Sinha SK, eds. *A Manual of Neonatal Respiratory Care*. New York: Futura Publishing, 2000:226–34
13. Pillow JJ, Neil H, Wilkinson MH, *et al.* Effect of I/E ratio on mean alveolar pressure during high frequency oscillatory ventilation. *J Appl Physiol* 1999;87:407–41
14. Courtney SE, Durand DJ, Asselin JM, *et al.* High frequency oscillatory ventilation versus conventional mechanical ventilation for very low birth weight infants. *N Engl J Med* 2002;347:643–52