

# High-Frequency Jet Ventilation Improves Gas Exchange in Extremely Immature Infants with Evolving Chronic Lung Disease

Richard Plavka, M.D., Ph.D.,<sup>1</sup> M. Dokoupilová, M.D.,<sup>1</sup> L. Pazderová, M.D.,<sup>1</sup>  
P. Kopecký, M.D.,<sup>1</sup> V. Sebroň, M.D.,<sup>1</sup> M. Zapadlo, M.D.,<sup>1</sup> and M. Keszler, M.D.<sup>2</sup>

## ABSTRACT

Extremely preterm infants often develop chronic lung disease (CLD) characterized by heterogeneous aeration; poorly supported, floppy airways; and air trapping. High-frequency jet ventilation (HFJV) with high end-expiratory pressure (optimal lung volume strategy [OLVS]) may improve airway patency, lead to better gas distribution, improve gas exchange, and facilitate extubation. In a pilot trial, this study sought to explore the effect of HFJV on oxygenation, ventilation, and ease of extubation in preterm infants with evolving CLD and refractory respiratory failure (RRF). From September 2002 to October 2004, 12 episodes of RRF developed in 10 ventilated extremely immature infants with evolving CLD (10 on conventional and two on high-frequency oscillation). Chorioamnionitis was confirmed in all infants, patent ductus arteriosus was ligated in five patients, and *Ureaplasma urealyticum* was cultured from trachea in four patients. HFJV with OLVS was initiated when oxygenation index (OI) > 10 or exhaled tidal volume (VTE)  $\geq$  7 mL/kg were required to maintain partial pressure of carbon dioxide, arterial (PaCO<sub>2</sub>) < 60 mm Hg. Inspiratory time (0.02/s) and frequency (310 to 420/min) were set initially with adjustment of pressure amplitude to keep PaCO<sub>2</sub> between 45 and 55 mm Hg. Ventilatory stabilization and weaning from mechanical ventilation with extubation to nasal continuous positive airway pressure (CPAP) were the goals of this approach. Gas exchange data were analyzed by Analysis of variance for repeated measures. Ten patients on 11 occasions of RRF were extubated to nasal CPAP successfully in a median of 15.5 days. Nine of 10 patients survived (one died of pentology of Cantrell), all required supplemental O<sub>2</sub> at 36 weeks. PaCO<sub>2</sub> decreased within 1 hour after the initiation of HFJV, and OI decreased by 24 hours. Both remained significantly lower until successful extubation ( $p < 0.02$ ). Compared with conventional ventilation or high-frequency oscillatory ventilation, HFJV used with OLVS appears to improve gas exchange and may facilitate weaning from mechanical ventilation (MV) in extremely immature infants with evolving CLD. These encouraging pilot data need to be confirmed in a larger clinical trial.

**KEYWORDS:** Chronic lung disease, high-frequency jet ventilation, gas exchange

<sup>1</sup>Division of Neonatology, Department of Obstetrics and Gynecology, 1st Medical Faculty, Charles University, Prague, Czech Republic;  
<sup>2</sup>Georgetown University, Washington, District of Columbia.

Address for correspondence and reprint requests: Richard Plavka, M.D., Ph.D., Department of Obstetrics and Gynecology, Division of Neonatology General Faculty Hospital in Prague, Charles University,

18 Apolinarska Street, 128 08 Prague 2, Czech Republic.

Am J Perinatol 2006;23:467-472. Copyright © 2006 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

Accepted: April 18, 2006. Published online: November 8, 2006.  
DOI 10.1055/s-2006-954821. ISSN 0735-1631.

Extremely preterm infants often develop chronic lung disease (CLD) characterized by heterogeneous aeration, poorly supported, floppy airways and air-trapping. Disruption of development of gas exchange units with partial/global respiratory failure, as a result of decreased alveolarization, as well as disturbed small airway function and inflammation, is the main cause of refractory respiratory failure (RRF) in infants with evolving CLD.<sup>1,2</sup> Increasing tidal volume (VT) and high fraction of inspired oxygen (FIO<sub>2</sub>) used during mechanical ventilation exacerbate the ventilator-induced injury leading to a vicious cycle. Despite the use of patient-triggered conventional ventilation (PT-CV) with the lung protective strategy using lower tidal volume and higher positive end-expiratory pressure (PEEP) with permissive hypercapnia, partial or global respiratory failure characterized by poorly compliant lungs and significantly increased airway resistance often develops.<sup>3</sup> This in turn leads to the need to increase VT above the physiological level and can cause volutrauma with possible development of air leak syndromes.<sup>4,5</sup>

High-frequency ventilation with lower tidal volume attenuates large volume changes associated with conventional ventilation and therefore it may decrease the incidence and severity of lung injury when applied early in the course of respiratory distress syndrome.<sup>6-8</sup> However, high-frequency oscillatory ventilation (HFOV) may further exacerbate respiratory failure in infants with evolving heterogeneous lung disease who have poorly supported small airways lacking intrinsic rigidity, and high airway resistance. HFOV appears to cause further air-trapping because of the active exhalation and relatively high inspiratory to expiratory (I:E) ratio (1:2 or 1:3).<sup>9,10</sup> Middle to lower level immature, floppy bronchi with disrupted architecture collapse easily, especially during active exhalation, which results in lower pressure in the airways than in the surrounding lung parenchyma. The problem commonly is exacerbated by the usual clinical response to radiographically documented air-trapping and hypercapnia; namely, reduction in distending airway pressure. The higher mean airway pressure needed to overcome the tendency of these airways to collapse during active exhalation may lead to circulatory adverse effects.

High-frequency jet ventilation (HFJV) delivers very small tidal volumes in a very short inspiratory time at high rates that allow exhalation time to be much longer than inspiratory time. The biophysical principle of HFJV is characterized by the axial jet stream of gas mixture reaching the alveolar spaces quickly during a very short inspiration, followed by spiral passive exhalation. It may thus provide superior alveolar ventilation and oxygenation, compared with other mechanical ventilatory modes, especially when small airway disease is the dominant pathophysiology.<sup>11</sup> Conversely, it must be recognized that CLD

typically is associated with increased airway resistance, which may increase the risk of air-trapping when rapid respiratory rate is used with any type of mechanical ventilation.

In a small retrospective analysis, Friedlich et al determined that the use of HFJV improved hypoxemic respiratory failure unresponsive to HFOV in very immature infants in whom evolving CLD was complicated by pneumonia or sepsis.<sup>12</sup> We decided to conduct a prospective observational pilot trial in which infants with evolving CLD were crossed over to HFJV from either conventional ventilation or HFOV at an earlier point in an early rescue mode when they experienced a requirement for increasing tidal volume and/or had a persistently increasing oxygenation index (OI) > 10. The objective was to explore the effect of HFJV on oxygenation, ventilation, and ease of extubation in preterm infants with evolving CLD and RRF.

## PATIENTS AND INTERVENTIONS

From September 2002 to October 2004, in the Tertiary Regional Neonatal Intensive Care Unit of the Perinatology Center in Prague (Czech Republic), 12 episodes of RRF developed in 10 mechanically ventilated extremely immature infants with median gestational age 23.6 weeks (range, 22 + 3/7 to 26 + 3/7 weeks) and median birth weight 650 g (range, 390 to 1020 g). All patients had received prophylactic surfactant (Curosurf 80 mg/mL; Chiesi Farmaceutici, Parma, Italy) in the delivery room. Subsequent doses of surfactant for CLD were not used. Echocardiographic evaluation for patent ductus arteriosus (PDA) was performed routinely and when present, the PDA was treated with indomethacin, followed by surgical ligation, if it remained refractory to medical therapy. Heterogeneous lung disease with evolving CLD was present in all patients. Six patients were on pressure support-volume guarantee mode, three patients were on synchronized intermittent mandatory ventilation-volume guarantee (SIMV-VG), two patients were on HFOV, and one patient was on SIMV. Chorioamnionitis was confirmed by placental histology in all cases, patent ductus arteriosus was ligated in five infants, and *Ureaplasma urealyticum* was cultured from the trachea in four patients. Eight infants were exposed to antenatal corticosteroids and five received a complete course. Demographic data and other key characteristics of study patients are presented in Table 1.

Lung protective, low-volume, high-PEEP strategy with permissive hypercapnia (range of target PaCO<sub>2</sub> was 50 to 55 mm Hg) was used on conventional modes (Dräger 8000 Plus, Draeger, Inc., Lubeck, Germany) and optimal lung volume strategy was used on HFOV (SensorMedics 3100A, SensorMedics, Inc., Yorba Linda, CA).

Table 1 Basic Demographic Data of Patients with Evolving CLD

Patient/ Sex	BW (g)	GA (wk)	CHAN (pos/neg)	PDA Ligation (yes/no)	<i>U. urealyticum</i> (pos/neg)	Doses of Surfactant (n)	X-ray*		Survival (yes/no)
							10th DOL	30th DOL	
1/F	490	23, 6	Pos	Yes	Pos	3	3-4	4	Yes
2/M	655	24, 1	Pos	Yes	Pos	1	2	3	Yes
3/M	650	23, 1	Pos	No	Neg	1	3	5	Yes
4/M	670	24, 3	Pos	Yes	Neg	1	1-2	2	Yes
5/M	1020	26, 3	Pos	No	Neg	3	3-4	4	No <sup>†</sup>
6/M	470	22, 3	Pos	Yes	Neg	3	3	3-4	Yes
7/F	390	23, 1	Pos	No	Pos	2	4-5	5	Yes
8/M	640	22, 4	Pos	No	Pos	3	1	3	Yes
9/M	600	25, 1	Pos	Yes	Neg	1	4	5	Yes
10/F	650	25, 2	Pos	No	Pos	1	3-4	4	Yes
Median	645	23, 6				1.5	3	4	
Range	390-1020	22.3-26.3				1-3	1-4.5	3-5.5	

\*Classification according to Weinstein.

<sup>†</sup>Congenital defect (pentology of Cantrell).

CLD, chronic lung disease; BW, birthweight; GA, gestational age; CHAN, chorioamnionitis; PDA, patent ductus arteriosus; DOL, day of life.

### INDICATIONS FOR CROSSOVER FROM PT-CV OR HFOV TO HFJV

HFJV was initiated when the following conditions were present:

1. Exhaled tidal volume ( $V_{TE}$ )  $\geq 7$  mL/kg with an adequate level of PEEP is not able to maintain  $P_{aCO_2} < 60$  torr or
2. OI is  $> 10$  and is increasing.

In addition to the above criteria, the following conditions had to be satisfied to ensure that ventilatory and supportive measures were optimized, and despite this, the infant's condition continued to deteriorate:

- Ventilation had been deteriorating progressively for 12 hours despite appropriate adjustments.
- Ventilation was unstable with fluctuating  $P_{aCO_2}$  in the range of 55 to 65 mm Hg during the last 24 hours.
- Oxygenation had been deteriorating for 24 hours.
- The patient had been sedated for at least 24 hours.

The Life Pulse jet ventilator (Bunnell Inc., Salt Lake, UT) was used for HFJV. The high-volume strategy with optimal lung inflation was the main principle of HFJV therapy, with adjustment of the pressure amplitude ( $\Delta P$ ) to achieve adequate ventilation of the thorax and maintain  $CO_2$  in a range 45 to 55 mm Hg. The inspiratory time of 0.02 seconds and frequency of 310 to 420/min were set initially. Ventilatory stabilization and weaning from mechanical ventilation with extubation to nasal continuous positive airway pressure (CPAP) were the goals of this approach. Low-dose, short-course of dexamethasone was considered only shortly before planned extubation to prevent airway obstruction due to edema. None of these patients

received corticosteroid treatment during the first 72 hours of HFJV.

### STATISTICAL ANALYSIS

This pilot study is descriptive in nature. Accordingly, primarily descriptive statistics are presented. Lack of published data in a similar population precludes a valid power analysis. Gas exchange data were analyzed by analysis of variance for repeated measures. A  $p$  value of  $< 0.05$  was considered significant.

### RESULTS

Nine of the 10 patients survived (patient 5 died from pentology of Cantrell at 336 days of life). Median postnatal age and median weight prior to HFJV were 19 days (range, 9 to 155 days) and 708 g (range, 575 to 4720 g). Two patients needed to be reintubated and ventilated by HFJV more than once. The median postnatal age of the first introduction of HFJV was 17.5 days (range, 9 to 39 days). On 10 occasions in eight patients, conventional modes were crossed over to HFJV. On four occasions in three patients, the primary indication for change to HFJV was inadequate  $CO_2$  removal despite tidal volumes  $\geq 7$  mL/kg. On seven occasions in six patients, oxygenation and ventilation had been gradually deteriorating and OI  $> 10$  was the primary indication for HFJV. Median PEEP,  $F_{IO_2}$ , and exhaled tidal volume ( $V_{TE}$ ) of conventional ventilation prior to switching were 7.0 cm  $H_2O$  (range, 6.1 to 10.0 cm  $H_2O$ ), 0.38 (range, 0.24 to 0.50 mL/kg), and 6.7 (range, 5.2 to 8.0 mL/kg), respectively. Mean airway pressure,  $F_{IO_2}$ , and VTE (measured by the Neonatal Respiration Monitor SLE 2100 VOM; SLE Limited, South Croydon, United Kingdom) on HFOV were

**Table 2** Patients Characteristics and Ventilatory Settings Prior to HFJV

Patient	Weight (g)	PNA	Mode of MV	PEEP	FiO <sub>2</sub>	VTE (mL/kg)	Paco <sub>2</sub> (torr)	OI
1	770	39	SIMV	6.1	0.45	Unknown	62	13.3
2	705	27	PSV-VG	6	0.30	6.5	59	11.5
3	665	18	PSV-VG	9	0.30	7	58	8.7
4	660	15	SIMV-VG	6.5	0.30	8	65	8.6
4*	1055	47	SIMV-VG	8.3	0.25	7	72	8.8
5	1000	16	PSV-VG	7	0.30	6.7	58	10.9
5*	4720	155	PSV-VG	10	0.50	5.2	86	22.9
6	600	32	HFOV	13 <sup>†</sup>	0.45	3.6 <sup>‡</sup>	63	12.4
7	400	16	SIMV-VG	7.5	0.50	6.3	56	15.4
8	575	9	HFOV	9 <sup>†</sup>	0.35	3.8 <sup>‡</sup>	66	5.5
9	710	20	PSV-VG	7	0.40	6.1	50	10.2
10	725	17	PSV-VG	7	0.40	7.0	43	8.3
Median	708	19		7	0.38	6.7	61	10.6
Range	575-4720	9-155		6.1-10.0	0.24-0.50	5.2-8.0	43-86	5.5-22.9

\*The second occasion in the same patient.

<sup>†</sup>Continual distending pressure.

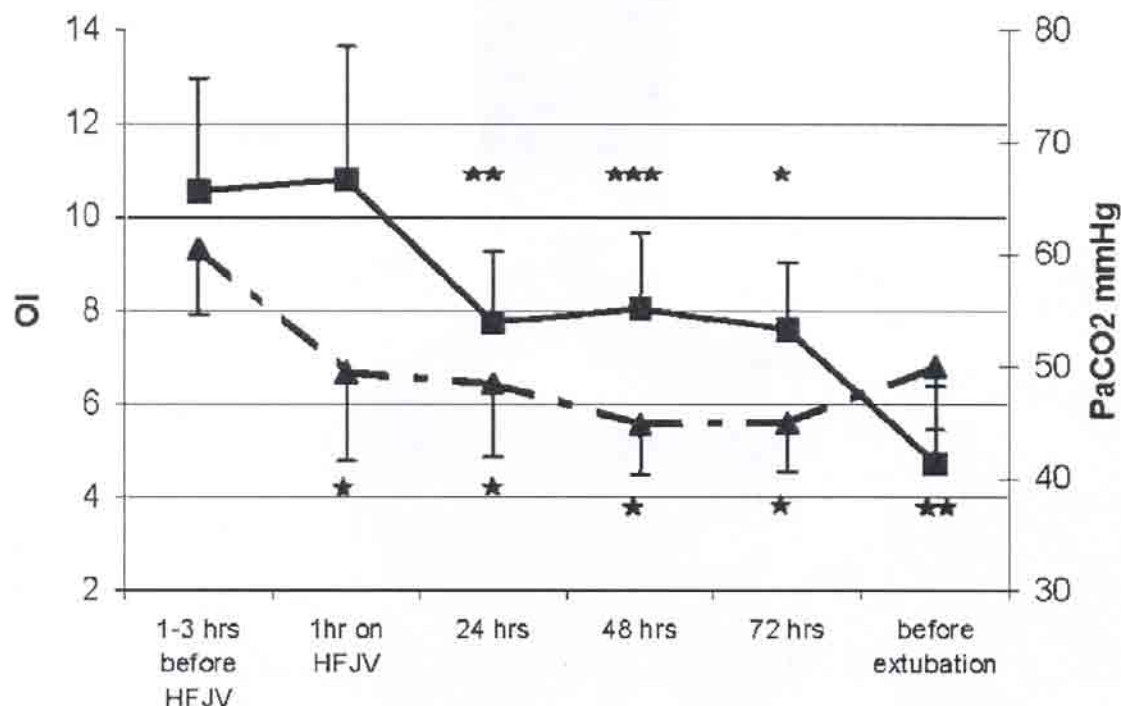
<sup>‡</sup>VTE on HFOV.

PNA, postnatal age; MV, mechanical ventilation; PEEP, positive end-expiratory pressure; FiO<sub>2</sub>, fraction of inspired oxygen; VTE, exhaled tidal volume; Paco<sub>2</sub>, partial pressure of carbon dioxide, arterial; OI, oxygenation index; PSV-VG, support-volume guarantee; SIMV-VG, synchronized intermittent mandatory ventilation-volume guarantee; HFOV, high-frequency oscillatory ventilation.

11.0 cm H<sub>2</sub>O, 0.40 mL/kg, and 3.7 mL/kg, respectively, before crossover to HFJV.

Patient characteristics and ventilatory settings prior to HFJV are shown in Table 2. The median OI decreased significantly during the first 24 hours of HFJV

(10.6 *v* 7.8; *p* < 0.015) and remained at this level for the next 48 hours, then decreased further to 4.8 prior to extubation (Fig. 1). Median Paco<sub>2</sub> levels decreased significantly from 61 to 50 mm Hg after 1 hour of HFJV (*p* < 0.001) and remained within target levels



**Figure 1** The squares are median values with 95% confidence limits of oxygenation index prior to and during 72 hours of high-frequency jet ventilation (HFJV) until extubation. The median oxygenation index decreased during the first 24 hours of HFJV significantly and remained significantly lower for the next 48 hours, then decreased further before extubation. The triangles are median values with 5% confidence limits of partial pressure of carbon dioxide, arterial (Paco<sub>2</sub>) prior to and during HFJV, and before extubation. The median Paco<sub>2</sub> decreased after 1 hour of HFJV and remained significantly lower until extubation (*p* < 0.001\* *p* < 0.015\*\* *p* < 0.03\*\*\*).

**Table 3** Initial HFJV Settings, and Ventilatory and Pulmonary Outcome

Patient	Paw	FiO <sub>2</sub>	PIP	Frequency	Duration of HFJV (d)	Successful Extubation from HFJV to NCPAP	Cumulative Dose of PNS (mg/kg)	Supplemental O <sub>2</sub> (d)	CLD*
1	11	0.40	20	420	16	Yes	0.24	130	Yes
2	11	0.40	25	350	2.5	Yes	0	105	Yes
3	12	0.25	25	350	15	Yes	0.80	93	Yes
4	10.5	0.35	22	310	22	Yes	0.82		
4 <sup>1</sup>	11	0.30	23	380	4	No	0	85	Yes
5	9.5	0.35	25	420	48	Yes	0.9		
5 <sup>1</sup>	14	0.50	37	340	8	Yes	1.5	336 <sup>2</sup>	Yes
6	9.6	0.21	21	380	5	Yes	0.6	111	Yes
7	10.8	0.50	25	320	35	Yes	1.33	125	Yes
8	9	0.25	22	370	27	Yes	0	86	Yes
9	8.6	0.40	17	320	73 <sup>3</sup>	Yes	0	125	Yes
10	9.5	0.40	20	380	5	Yes	0	72	Yes
Median	10.7	0.38	23	360	15.5			108	
Range	8.6-14	0.21-0.5	17-37	310-420	2.5-73			72-336	

\*Supplemental oxygen requirement at week 36.

<sup>1</sup>The second occasion in the same patient.

<sup>2</sup>Died of congenital defect (pentology of Cantrell).

<sup>3</sup>Late extubation due to laryngomalacia.

Paw, mean airway pressure; FiO<sub>2</sub>, fraction of inspired oxygen; PIP, peak inspiratory pressure; HFJV, high-frequency jet ventilation; NCPAP, nasal continuous positive airway pressure; PNS, postnatal corticosteroids (dexamethasone); CLD, chronic lung disease.

until extubation (Fig. 1). Ten patients on 11 occasions of RRF were extubated to nasal CPAP successfully. On one occasion, the infant was weaned to SIMV-VG mode after 48 hours of HFJV because of a technical problem with the jet ventilator. Median length of HFJV was 15.5 days. HFJV was prolonged for nonpulmonary reasons in two patients. Patient 5 had impaired diaphragm fixation due to congenital defect (pentology of Cantrell) and laryngomalacia occurred in patient 9. Postnatal low-dose, short-course dexamethasone was started before extubation in six infants. All infants required oxygen supplementation at 36 postconceptional weeks with median duration of oxygen requirement 108 days (range, 72 to 336 weeks). The initial HFJV settings, and ventilatory and pulmonary outcome are documented in Table 3.

Two infants had moderate and two had mild neurosensory abnormality at age 2 years. Three are classified as a normal at age 2 years and two had normal neurosensory development at age 18 months.

## DISCUSSION

Improved gas exchange with ventilatory stabilization was achieved in all of our extremely immature infants after the introduction of HFJV. Nine infants survived with successful extubation from HFJV to nasal CPAP. The low-dosage corticosteroid course was administered in six patients before extubation. The significant decrease of OI just before extubation could be related in part to this treatment, but the bulk of the improvement in gas exchange occurred before the short course of cortico-

steroids was started. All patients were high risk for the development of CLD. They needed to be mechanically ventilated and had been exposed to histologically confirmed chorioamnionitis; five of them had positive culture of *U. urealyticum* from tracheal aspirate. Patent ductus arteriosus needed to be ligated in five infants. The radiographic staging documented that the microcystic stage developed in seven infants.

Infants with heterogeneous lung disease, inflammatory changes, poorly supported airways and elevated airway resistance are difficult to ventilate and oxygenate optimally. We attempted to use the most lung-protective strategy possible by optimizing lung volume and limiting tidal volume.<sup>13,14</sup>

The adjustment of PEEP level was the first step to optimize lung inflation and reach a larger surface area for gas exchange. Mild overexpansion of the lungs was a second reason for increasing PEEP. This response is contrary to common practice, but is based on sound pathophysiologic principles. The poorly supported floppy airways of extremely preterm infants are susceptible to collapse in the latter stages of exhalation as lung volume decreases. The air-trapping that is commonly seen in these patients can often be reduced by modest increase in PEEP, which serves to splint the airways open. The other key aspect of our approach was to avoid the use of excessive tidal volumes above the physiological range on conventional ventilation. The more heterogeneous the lung becomes with increased number of compartments with different time constants, the higher the tidal volumes needed for gas exchange during conventional ventilation, where the

bulk flow (convection) is the dominant factor determining ventilation to the different regions of lungs. This was the reason for using a requirement for supraphysiologic tidal volume as a criterion for initiation of HFJV.

The mechanisms of gas transport during high frequency ventilation, such as flow streaming with augmented dispersion and Pendelluft effect, can facilitate diffusion and gas exchange in compartments with different time constants. We believe that these mechanisms may explain the improvement in both oxygenation and ventilation after the crossover from conventional modes to high-frequency ventilation.<sup>15</sup> Two patients who were switched from HFOV to HFJV both had increasing CO<sub>2</sub> levels with evidence of overinflation. Despite attempts during HFOV to lower the oscillatory frequency to 8 Hz and adjustment of continuous distending pressure to achieve optimum lung inflation, partial derecruitment with choke points and overinflation with gas-trapping could not be avoided. We speculate that the tiny, poorly supported airways of these extremely premature infants are prone to collapse during active expiration on HFOV. Active exhalation results in airway pressure that is lower than that of the surrounding lung parenchyma, which causes the small airways, which have no intrinsic rigidity, to collapse, creating so-called choke points. HFJV appears to provide better management of optimal lung volume because the expired gases swirl out from airways passively with a longer expiration time. The much lower I:E ratio on HFJV (1:7 to 1:10) can minimize gas-trapping and in many instances improves gas exchange quickly in infants with evolving CLD.

All surviving infants required a modest amount of oxygen supplementation at 36 postconceptional weeks; seven were weaned successfully to room air before 40 postconceptional weeks and were able to be discharged home without oxygen. HFJV appears to be superior to conventional modes and to HFOV, due to better distribution of gas with improvement of oxygenation and ventilation in infants with evolving CLD. The optimal timing of HFJV indication and the impact on long term outcome of extremely immature infants is unclear.

## CONCLUSION

Compared with conventional ventilation or HFOV, HFJV used with optimal lung volume strategy appears to improve gas exchange and may facilitate weaning from mechanical ventilation in extremely immature infants with evolving CLD. These encouraging pilot data need to be verified in a larger clinical trial.

## ACKNOWLEDGMENT

Supported by Internal Grant Agency of Ministry of Health, Czech Republic, NR8360-2.

## REFERENCES

1. Coalson JJ, Winter V, deLemos RA. Decreased alveolarization in baboon survivors with bronchopulmonary dysplasia. *Am J Respir Crit Care Med* 1995;152:640-646
2. Coalson JJ, Winter VT, Siler KT, Yoder BA. Neonatal chronic lung disease in extremely immature baboons. *Am J Respir Crit Care Med* 1999;160:1333-1346
3. Rimensberger PC. Neonatal respiratory failure. *Curr Opin Pediatr* 2002;14:315-321
4. Muscedere JG, Mullen JBM, Gan K, Slutsky AS. Tidal volume at low airway pressures can augment lung injury. *Am J Respir Crit Care Med* 1994;149:1327-1334
5. Ito Y, Manwell SEE, Kerr CL, et al. Effects of ventilation strategies on the efficacy of exogenous surfactant therapy in a rabbit model of acute lung injury. *Am J Respir Crit Care Med* 1998;157:149-155
6. 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;98:1044-1052
7. Plavka R, Kopecky P, Sebron V, Svihovec P, Zlatohlavkova B, Janus V. A prospective randomized comparison of conventional mechanical ventilation and very early high frequency oscillatory ventilation in extremely premature newborns with respiratory distress syndrome. *Intensive Care Med* 1999;25:68-75
8. 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;347:643-652
9. Solway J, Rossing TH, Saari AF, Drazen JM. Expiratory flow limitation and dynamic pulmonary hyperinflation during high frequency ventilation. *J Appl Physiol* 1986;60:2071-2078
10. Pillow JJ, Neil H, Wilkinson MH, Ramsden CA. Effect of I/E ratio on mean alveolar pressure during high frequency oscillatory ventilation. *J Appl Physiol* 1999;87:407-441
11. Bunnell JB. General concepts of high frequency ventilation. In: Donn SM, Sinha SK, eds. *A Manual of Neonatal Respiratory Care*. New York: Futura Publishing Co; 2000:226-234
12. Friedlich P, Subramanian N, Sebald M, Noori S, Seri I. Use of high-frequency jet ventilation in neonates with hypoxemia refractory to high-frequency oscillatory ventilation. *J Matern Fetal Neonatal Med* 2003;13:398-402
13. Clark RH, Gerstmann DR, Jobe AH, Moffitt ST, Slutsky AS, Yoder BA. Lung injury in neonates: causes, strategies for prevention, and long-term consequences. *J Pediatr* 2001;139:478-486
14. van Kaam AH, Haitsma JJ, De Jaegere A, van Aalderen WM, Kok JH, Lachmann B. Open lung ventilation improves gas exchange and attenuates secondary lung injury in a piglet model of meconium aspiration. *Crit Care Med* 2004;32:443-449
15. Dos Santos CC, Slutsky AS. Overview of high-frequency ventilation modes, clinical rationale, and gas transport mechanisms. *Respir Care Clin N Am* 2001;7:549-575