Multicenter controlled trial comparing high-frequency jet ventilation and conventional mechanical ventilation in newborn infants with pulmonary interstitial emphysema

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One hundred forty-four newborn infants with pulmonary interstitial emphysema were stratified by weight and severity of illness, and randomly assigned to receive treatment with high-frequency jet ventilation (HFJV) or rapid-rate conventional mechanical ventilation (CV) with short inspiratory time. If criteria for treatment failure were met, crossover to the alternate ventilatory mode was permitted. Overall, 45 (61%) of 74 infants met treatment success criteria with HFJV compared with 26 (37%) of 70 treated with CV (p <0.01). Eighty-four percent of patients who crossed over from CV to HFJV initially responded to the new treatment, and 45% ultimately met success criteria on HFJV. In contrast, only 9% of those who crossed over from HFJV to CV responded well to CV (p <0.01), and the same 9% ultimately met success criteria (p <0.05). Therapy with HFJV resulted in improved ventilation at lower peak and mean airway pressures, as well as more rapid radiographic improvement of pulmonary interstitial emphysema, in comparison with rapid-rate CV. Survival by original assignment was identical. When survival resulting from rescue by the alternate therapy in crossover patients was excluded, the survival rate was 64.9% for HFJV, compared with 47.1% for CV (p <0.05). The incidence of chronic lung disease, intraventricular hemorrhage, patent ductus arteriosus, airway obstruction, and new air leak was similar in both groups. We conclude that HFJV, as used in this study, is safe and is more effective than rapid-rate CV in the treatment of newborn infants with pulmonary interstitial emphysema. (J PEDIATR 1991;119:85-93)

Diffuse pulmonary interstitial emphysema is a common and serious complication of mechanical ventilation in infants with the respiratory distress syndrome.[1-3] Conventional treatment typically employs rapid intermittent mandatory ventilation and short inspiratory time in an effort to minimize airway pressures.[4] Despite these measures, the mor-

BPD	Bronchopulmonary dysplasia
CV	Conventional mechanical ventilation
Fio$_2$	Fractional inspired oxygen
HFJV	High-frequency jet ventilation
IMV	Intermittent mandatory ventilation
Paco$_2$	Arterial carbon dioxide partial pressure
Pao$_2$	Arterial oxygen partial pressure
P$\overline{aw}$	Mean airway pressure
PEEP	Positive end-expiratory pressure
PIE	Pulmonary interstitial emphysema
PIP	Peak inspiratory pressure

tality rate remains high and chronic lung disease is a common sequela.[5-8] High-frequency jet ventilation has been shown to provide effective gas exchange at lower airway pressures than conventional mechanical ventilation[9-14] and thus might prove to be beneficial in the presence of an air leak. Uncontrolled reports of successful rescue with HFJV of moribund infants with PIE support this hypothesis,[15-18] but to date no controlled study has been published. In this report we present the results of a prospective, multicenter, collaborative clinical trial designed to evaluate the safety and efficacy of HFJV in newborn infants with PIE.

METHODS

Patient selection. All newborn infants less than 7 days of age and weighing ≥750 gm at birth, in whom PIE developed during CV, were considered for entry into the study regardless of the severity of their respiratory illness. Babies with congenital anomalies, grade III or IV intraventricular or periventricular hemorrhage documented before entry, perinatal asphyxia (defined arbitrarily as a 5-minute Apgar score <3), severe neutropenia (absolute neutrophil count <1000 cells/mm^3), lack of arterial access, and those infants who could not undergo placement of a Hi-Lo triple-lumen endotracheal tube (Mallinckrodt, Inc., St. Louis, Mo.) were excluded.

Study design and sample size. The study protocol was approved by the institutional review board of each of the participating centers. Eligible patients whose parents gave written informed consent were stratified by birth weight (<1000 gm, 1000 to 1500 gm, >1500 gm) and by severity of illness. Babies were classified as having *less severe* illness if they had both unilateral PIE diagnosed beyond 24 hours of age and P$\overline{aw}$ <12 cm H$_2$O. Any baby who had P$\overline{aw}$ ≥12 cm H$_2$O was classified as having *more severe* illness, as were all those with either bilateral or unilateral PIE diagnosed before 24 hours of age. The patients were then randomly assigned to receive HFJV or continued CV, with a separate table of random numbers used for each of the six stratification groups to ensure balanced allocation to the two arms of the study. Randomization was performed centrally by means of a 24-hour hotline.

Ethical considerations relating to high mortality rates in newborn infants with PIE and available anecdotal evidence of possible benefit of HFJV precluded a simple randomization with death as a possible end point. Consequently, if specific criteria for treatment failure were met, crossover to the other arm of the study was permitted as a rescue maneuver. Thus the major outcome variable was the success or failure of the originally assigned therapy and response to the alternate therapy after crossover.

The criteria for *treatment success* were (1) resolution of PIE for ≥24 hours and (2) substantial radiographic improvement of PIE and reduction of P$\overline{aw}$ to 40% less than baseline values recorded before initiation of the study.

Criteria for *treatment failure* were (1) worsening PIE, as demonstrated by significant radiographic worsening of PIE or development of intractable air leaks, accompanied by deteriorating gas exchange requiring increasing ventilatory support to maintain target blood gas values (an increase of ≥10% in peak inspiratory pressure, or P$\overline{aw}$ was considered a significant increase); (2) lack of improvement, defined as no improvement of PIE after 96 hours, accompanied by deteriorating gas exchange (as defined above); (3) inadequate gas exchange during maximal support, including arterial oxygen tension <40 mm Hg, or arterial carbon dioxide tension >65 mm Hg on P$\overline{aw}$ >15 cm H$_2$O and fraction of inspired oxygen = 1.0; and (4) acute deterioration, demonstrated by sudden worsening of the patient's status, so that continued participation in the study would be contrary to his or her best interest. Acute, transient deterioration secondary to reversible phenomena such as pneumothorax or mechanical problems with the ventilator, circuit, and so forth were not considered criteria for failure. Once a patient was removed from the study on the basis of either treatment success or failure, the clinician was free to choose the mode of ventilation to be used.

Analysis of statistical power was based on an α level of 0.05, 1-β of 0.80, and a moderate treatment effect. On the basis of published data and recent institutional experience, we anticipated an incidence of failure of initial therapy of approximately 60%. Thus, with a two-sided test, an estimated 200 patients would be needed to detect, with 80% probability, a difference of 20 percentage points in the incidence of failure of the initially assigned therapy.

Ventilators and ventilator strategies. For patients assigned to HFJV, the Life Pulse high-frequency jet ventilator (Bunnell Inc., Salt Lake City, Utah) was used. This device senses airway pressures near the tip of the endotracheal tube, and a microprocessor servocontrols driving gas pressure to maintain the desired peak inspiratory pressure.[19] The ventilator has an effective gas heating and humidification system and a number of carefully designed safety features. A conventional ventilator used in tandem with the Life Pulse ventilator is a source of bias flow of heated, humidified gas of the same Fio$_2$ as the jet ventilator. The con-
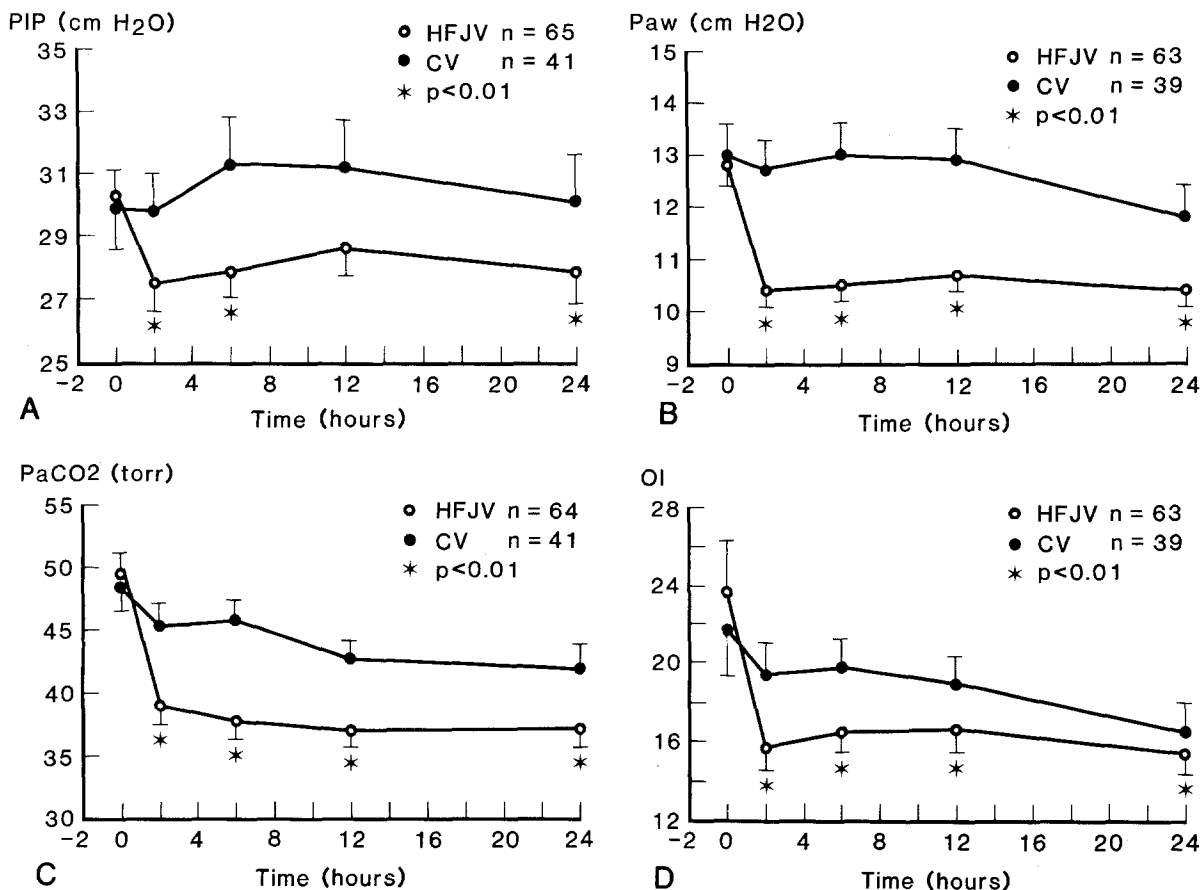
Fig. 1. Peak inspiratory pressure (A), mean airway pressure (B), $PaCO_2$ (C), and oxygenation index (D) for the first 24 hours of the study. Data are expressed as mean $\pm$ SEM.

ventional ventilator generates positive end-expiratory pressure and provides intermittent sigh breaths in the form of background IMV.

For this study the Life Pulse jet ventilator was initially set at 400 to 450 cycles/min with an inspiratory time of 0.02 second. The FIO_2 and PEEP were unchanged from baseline pre-HFJV values, and PIP was set at 10% to 20% below that measured just before the start of HFJV. Background IMV on the conventional ventilator was maintained at 5 to 10 breaths/min with an inspiratory time of 0.3 to 0.5 second. The peak pressure of the background IMV was set approximately 5 cm H_2O below the peak pressure of the Life Pulse ventilator. This strategy allows the jet ventilator "breaths" to superimpose onto the background IMV without exceeding the PIP safety limit and interrupting the cycling of the jet ventilator. Background IMV was omitted in patients with radiographic evidence of gross overexpansion of the lungs.

Initial ventilator settings were adjusted in response to arterial blood gas values and clinical observation of the adequacy of chest wall movement. Control of $PaCO_2$ was primarily achieved by changes in tidal volume as determined

by the difference between PIP and PEEP. Cycling frequency has relatively little effect on carbon dioxide elimination and generally remained in a narrow range of 400 to 450 cycles/min. Oxygenation was controlled by changes in FIO_2 and $\overline{Paw}$. End-expiratory pressure was maintained at ≤ 6 cm H_2O and inspiratory time at 0.02 to 0.03 second. Consequently, $\overline{Paw}$ was primarily determined by PIP. Alternately, $\overline{Paw}$ could be raised by increasing the rate of background IMV to a maximum of 20 breaths/min.

Because of limited availability of the jet ventilator, patients who were successfully treated with HFJV were usually returned to CV once success criteria were met. At that point the $\overline{Paw}$ would be substantially lower than during the acute stage of the illness and a return to CV was considered appropriate and safe. For babies assigned to receive CV, time-cycled, pressure-limited ventilators (Bear Cub [Bear Medical Systems Inc., Rancho Cordova, Calif.], Sechrist [Seachrist Industries Inc., Anaheim, Calif.], or Baby Bird [Bird Products Corp., Palm Springs, Calif.]) were used, with an IMV rate of 60 to 100 breaths/min, inspiratory time of 0.20 to 0.35 second, expiratory time ≥ 0.3 second, and PEEP of ≤ 5 cm H_2O. The PIP settings were

Table I. Primary and secondary diagnoses, gender, and inborn/outborn ratio in the control and study groups

	CV* (n = 70)		HFJV* (n = 74)	
	No.	%	No.	%
Primary diagnosis of RDS	69	98.6	71	95.9
Air leak (other than PIE)	29	41.4	35	47.3
PDA	23	32.9	22	29.7
IVH	14	20.0	19	25.6
Sepsis	7	10.0	6	8.1
Pulmonary hypertension	2	2.9	2	2.7
Male gender	39	55.7	48	64.9
Inborn	40	57.1	41	55.4

RDS, Respiratory distress syndrome; *PDA*, patent ductus arteriosus; *IVH*, intraventricular hemorrhage
*No statistically significant differences.

guided by adequacy of chest wall movement and gas exchange.

Because of the presence of airleak, the ventilatory strategy in both groups was to minimize airway pressures even at the cost of requiring generous FIO_2. The target blood gas values for both groups were PaO_2 50 to 65 mm Hg, $PaCO_2$ 40 to 50 mm Hg, and pH 7.25 to 7.40.

General supportive neonatal care. Infants received neonatal care in accordance with standard practice in the respective neonatal intensive care units. None received exogenous surfactant. No attempt was made to control nonrespiratory aspects of care. Muscle relaxants were seldom given, and their use was at the discretion of the clinician. Symptomatic patent ductus arteriosus was treated with indomethacin or surgical ligation. Hypotension was treated with volume expansion and inotropic agents at the discretion of the clinical team.

Data collection and analysis. After randomization, all babies underwent reintubation with the triple-lumen Hi-Lo endotracheal tube so that airway pressures could be monitored near the tip of the endotracheal tube in both groups. Airway pressures were monitored with either the built-in airway pressure monitor of the Life Pulse ventilator or the freestanding Bunnell ventilator monitor. Both devices sample airway pressures every 1 or 2 milliseconds and have been shown to have an adequate frequency response over the clinically applicable range of frequencies.[20, 21]

After reintubation, baseline airway pressures, vital signs, and blood gas values were recorded while prestudy CV settings were maintained, and only then was HFJV or rapid-rate IMV initiated. Airway pressures, blood gas values, and vital signs were recorded every 2 hours during the study for a minimum of 72 hours. A chest radiograph was also obtained at the time of initial reintubation. Subsequent radiographs were obtained every 12 hours for 24 hours, and daily thereafter. Additional x-ray studies were performed as clinically indicated. A cranial sonogram was obtained within 12 hours before entry into the study whenever possible, then at 4 to 7 days, and again before discharge. Echocardiograms were obtained only when clinically indicated for suspected patent ductus arteriosus.

Categoric data were analyzed by chi-square or Fisher exact probability test. Data that were not normally distributed (time to failure, time to improvement and to resolution of PIE, and time to extubation) were analyzed with the Mann-Whitney test. Normally distributed numeric data were analyzed by unpaired t test. Airway pressure, vital signs, and blood gas data were compared by analysis of variance for repeated measures and two-way analysis of variance. The incidence of complications was calculated on the basis of the original group assignment.

Safety considerations and quality control. All participating centers had at least some prior experience with HFJV and with the Life Pulse ventilator. Additional in-service training for nurses, respiratory therapists, and physicians was provided as deemed necessary because of new staff, staff turnover, or any other reason. The choice of the jet ventilator to be used in the study was based in large measure on the carefully designed safety features of the Life Pulse ventilator and extensive experience with this device during earlier, uncontrolled rescue studies.[18, 22] The ventilator's humidification system was also regarded as highly desirable in view of indications that inadequate humidification of the ventilating gas might lead to tracheal damage.[23]

A four-member coordinating committee was charged with overseeing the protocol execution and accuracy of data collection by means of on-site visits and by telephone. The accuracy of all entries on the data collection forms was cross-checked against the original flow sheets before being entered into the data base. At the time of important decision points, such as initial diagnosis of PIE and subsequent determination of a significant change, the diagnosis was verified by a radiologist or another clinician not involved in the care of the patient to ensure objectivity in the interpretation of the chest radiographs. Interim analysis of the data was performed after approximately every 75 patients, to guard against excess complications and to avoid exposing babies needlessly to the inferior therapy if the advantage of one treatment modality was clearly demonstrated with a p value <0.01. The second such interim analysis led to the termination of the study in March 1989 because of the demonstrated superiority of HFJV.

RESULTS

One hundred sixty-six patients were entered into the study between January 1987 and March 1989. Twenty-two
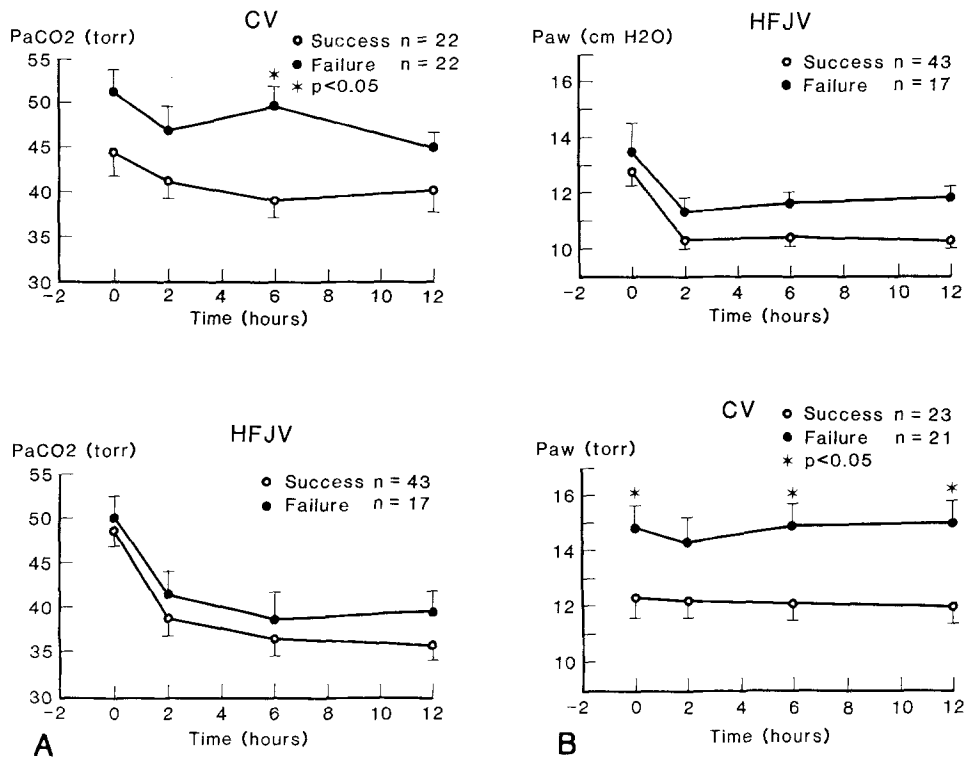
Fig. 2. $Paco_2$ (A) and mean airway pressure (B) for first 12 hours of study according to eventual outcome in terms of success or failure of initially assigned therapy. Data are expressed as mean ± SEM.

Table II. Patient characteristics, blood gas values, and ventilatory settings at entry into the study (baseline)

	CV* (n = 70)	HFJV* (n = 74)
Birth weight (gm)	1346 ± 523	1331 ± 515
Gestational age (wk)	29.3 ± 3.1	29.3 ± 3.1
Age at start of therapy (hr)	44.2 ± 28.7	49.4 ± 37.4
Pao_2 (mm Hg)	68.1 ± 37.8	68.9 ± 38.8
$Paco_2$ (mm Hg)	50.2 ± 14.1	51.1 ± 13.3
Fio_2	0.93 ± 0.12	0.93 ± 0.14
PIP (cm H_2O)	30.4 ± 7.3	30.4 ± 7.0
IMV (breath/min)	79.1 ± 23.1	76.7 ± 18.0
Oxygenation index ($\overline{Paw} \times Fio_2 \times 100/Pao_2$)	23.6 ± 14.3	24.1 ± 21.3

Values are expressed as mean ± SD.
*No statistically significant differences.

were eliminated from further consideration because of the presence of unrecognized exclusion criteria (9 patients), significant deviation from protocol (8), presence of a conflicting research protocol (3), or other reasons (2). Thus 144 patients were included in the final analysis. One hundred thirty patients (90%) were classified as having "more severe" illness. Because of the small number of subjects in the "less severe" category, their data are not presented separately. Seventy infants were assigned to CV and 74 were assigned to HFJV. There were no significant intergroup differences in the male/female ratio, primary diagnosis, or

comorbidity (Table I). The birth weight, gestational age, age at entry into the study, baseline ventilator settings, airway pressures, and blood gas values were also similar in the two groups (Table II)

Sixty-one percent of babies treated with HFJV met criteria for treatment success, compared with 37% of those assigned to CV (p <0.01). Babies with more severe illness met success criteria 61% of the time with HFJV, compared with 31% of the time with CV (p <0.01). Eighty-four percent of patients whose initially assigned treatment failed and who crossed over from CV to HFJV initially responded to the

Table III. Response to therapy

| | CV | | HFJV | |
	Median (Range)	n	Median (Range)	n
Time to improve PIE (hr)	53 (4-160)†	27	33 (2-144)†	44
Time to resolve PIE (hr)	70.5 (8-208)	24	75 (12-235)	33
Time to failure (hr)	8.5 (0.5-86)*	40	57 (2-242)*	23
Time to extubation (hr)	340 (87-5040)	32	325 (90-1764)	41

n, Number of available observations.
*$p < 0.01$.
†$p < 0.05$.

Table IV. Success of therapy, survival, and complications by birth weight

| | Birth weight (gm) | | | | | | | | |
| | <1000 | | | 1000-1500 | | | >1500 | | |
No. of cases	CV 24	HFJV 26	Total* 50	CV 25	HFJV 24	Total* 49	CV 21	HFJV 24	Total* 45
Success (%)	33	46	40	28†	63†	45	52	75	64
Survival (%)‡	33	35	40	44†	79†	78	57	83	87
BPD (%)	91	67	80	78	70	73	42	25	33
Alive, free of BPD (%)	4	12	8	16	25	20	52	63	58
IVH grades III, IV (%)	40	43	41	41	27	34	9	4	6

IVH, Intraventricular hemorrhage.
*Overall survival rate.
†$p < 0.05$.
‡Survival attributable to each type of ventilator (i.e., survival resulting from rescue by the alternative therapy in crossover patients has been excluded from the CV and HFJV columns).

new treatment, and 45% ultimately met success criteria on HFJV. In contrast, only 9% of those who crossed over from HFJV to CV responded well to CV ($p < 0.01$), and the same 9% ultimately met success criteria ($p < 0.05$). The pattern of a greater rate of success with HFJV, although consistent across all birth weight groups, was statistically significant only in the group weighing 1000 to 1500 gm. Of 44 infants who met success criteria during HFJV and were then returned to CV, 21 had a recurrence or worsening of PIE or substantial clinical deterioration or both within 48 hours of returning to CV. This proportion was significantly higher than that of infants who met success criteria during CV (5/ 26, $p < 0.05$). The most frequent criterion for failure was inadequate gas exchange despite maximal support (59%), followed by acute deterioration (19%), worsening PIE (17%) and failure to improve (5%). Ninety-four percent of patients who met success criteria survived; 89% of those whose initial therapy failed and who either were not offered the other modality or again met failure criteria after crossover died. These findings validate the success and failure criteria used in this study.

High-frequency jet ventilation resulted in more rapid improvement of PIE than did CV, and babies who ulti-

mately reached criteria for treatment failure did so more rapidly during CV than during HFJV (Table III). The time to complete resolution of PIE and the total duration of ventilator support did not differ significantly. High-frequency jet ventilation resulted in improved ventilation and in lower peak and mean airway pressures than did CV. The Pa_{O_2} and F_{IO_2} were similar in the two groups, so the oxygenation index (OI = $F_{IO_2} \times \overline{Paw} \times 100/Pa_{O_2}$) was also significantly improved in the HFJV group as a result of the lower $\overline{Paw}$ (Fig. 1). The mean IMV during the first 24 hours of CV ranged from 76 to 81 $\pm$ 20 breaths/min, and the mean frequency of the Life Pulse ventilator varied between 433 and 438 $\pm$ 50 cycles/min. There were no differences in heart rate or blood pressure between the HFJV and CV groups at baseline and at 2, 12, and 24 hours after the start of the study (data not shown).

The overall survival rates of 97 (67.4%) of the 144 patients did not differ between the two groups. However, when survival resulting from rescue by the alternate therapy in crossover patients was excluded, the survival rate was 64.9% for HFJV and 47.1% for CV ($p < 0.05$). The impact of HFJV on survival was most evident in the 1000 to 1500 gm infants (79% with HFJV vs 44% with CV; $p < 0.05$)

Table V. Incidence of major complications according to initially assigned therapy

	CV		HFJV		
	No.	**%**	**No.**	**%**	***p***
BPD in survivors	32/48	66.7	25/49	51.0	0.17
Symptomatic PDA	10/70	14.3	12/74	16.2	0.93
Total IVH (grades III, IV)	19/55	34.5	16/63	25.4	0.38
New IVH (grades III, IV)	10/44	22.7	6/54	11.1	0.20
New air leak	25/70	35.7	20/74	27.0	0.35
Airway obstruction	1/70	1.4	4/74	5.4	0.22
NTB at autopsy	2/8	25.0	3/9	33.3	0.69

The denominator represents the number of valid observations.
PDA, Patent ductus arteriosus; *IVH*, intraventricular hemorrhage; *NTB*, necrotizing tracheobronchitis.

(Table IV). As anticipated, survival positively correlated with birth weight, and the incidence of complications had a negative correlation (Table IV).

The initial response to treatment with HFJV, as reflected by improved ventilation and lower airway pressures during the first 12 hours of therapy, was favorable in almost all patients, regardless of eventual outcome. In contrast, the response of infants treated with CV differed significantly by 6 hours of therapy between the infants who eventually met success criteria and those babies in whom treatment subsequently failed (Fig. 2).

Bronchopulmonary dysplasia, defined as ventilator or oxygen requirement at 28 days of age with compatible radiographic changes, was diagnosed in 51% of surviving HFJV patients and 67% of CV survivors (*p* = 0.17). The incidence of major intraventricular hemorrhage, symptomatic patent ductus arteriosus, new air leak, clinically significant airway obstruction, and autopsy-documented necrotizing tracheobronchitis was similar in the two groups (Table V).

DISCUSSION

Pulmonary interstitial emphysema is a common complication of positive-pressure ventilation in preterm infants with respiratory distress syndrome. Surfactant therapy reduces but does not eliminate this ominous complication.[24, 25] Overall mortality rates of 45% to 54% have been reported with conventional treatment.[5] Factors contributing heavily to death include birth weight <1500 gm, development of PIE within the first 24 hours of life, and ventilatory requirements exceeding peak inspiratory pressures of 25 cm H_2O on the first day of life.[5] The majority of patients in our study met at least two of these conditions.

Our findings confirm previous reports of the benefits of HFJV compared with rapid-rate CV in the treatment of newborn infants with pulmonary air leaks. Pulmonary interstitial emphysema improved more rapidly and more often with HFJV at the time of initial treatment and again after crossover. As previously documented by Carlo et al.[9, 13] and others,[10-12] gas exchange was improved despite lower airway pressures. The overall survival rate of nearly 70% in this group of critically ill infants appears encouraging compared with recent reported experience.[3, 5] More important, the survival rate attributable to HFJV was significantly higher than that of babies who underwent CV, especially those who weighed between 1000 and 1500 gm at birth.

Unlike the collaborative HI-FI Study Group,[26] we found no increase in the incidence of complications. These contrasting results may be due to fundamental differences in the mechanism of gas delivery between jet ventilators and oscillators, to differences in ventilator strategy between the two clinical trials, or to differences in the populations under study. These considerations underscore the dangers of generalizing the conclusions of any study to different populations, disease processes, or treatment strategies, or to related but fundamentally different devices. Therefore it must be emphasized that this study compared HFJV with one specific strategy of CV. The rapid-rate CV technique was chosen because it appears to be most prevalent in clinical practice and is widely believed to be most efficacious in the presence of an air leak. However, it is conceivable that other CV strategies may have yielded different results.

Although reduction of the incidence of bronchopulmonary dysplasia was not the primary focus of this study, such reduction is believed to be an important potential benefit of HFJV. There are several possible reasons for the inconclusive findings with respect to BPD. First, there may in fact be no advantage to HFJV in preventing BPD; the study, however, does not have sufficient statistical power to accept the null hypothesis with confidence. Additionally, the ability to demonstrate an advantage of one or the other ventilator in reducing important complications was hampered by the crossover study design. The frequent clinical or radiographic deterioration on the return to CV after successful treatment with HFJV may have further limited our ability

to demonstrate a possible advantage of HFJV in the prevention of BPD, and suggests that early return to CV should be avoided. Finally, intervention in this population of infants with severe respiratory failure and established barotrauma may have come too late to have an impact on the incidence of BPD. The question of prevention of chronic lung disease can be adequately addressed only by a large collaborative study of the early application of HFJV.

Our finding of a 5.4% incidence of symptomatic airway obstruction is similar to the 3.3% reported by Mammel and Boros[27] and further supports recent evidence that HFJV does not cause a disproportionate amount of airway damage.[28] Also analogous to the observations of Mammel and Boros was our finding of a relatively high incidence of histologic evidence of necrotizing tracheobronchitis in the absence of clinical signs of airway obstruction. The relatively low autopsy rate in our patients and the fact that virtually all those patients had been exposed to both ventilators make specific conclusions regarding airway damage difficult. However, our findings are consistent with other recent reports which show that airway damage is a common complication of all forms of mechanical ventilation and is, at least in part, caused by coexisting hypoxia and hypotension, which are so prevalent in this population.[29-31]

This study was designed to address the specific issue of the efficacy of HFJV in the treatment of PIE. To that end, a particular ventilator strategy was employed. This strategy emphasized reduction of airway pressures as its primary objective and accepted the trade-off of a relatively high FIO_2 requirement. This strategy appears to be appropriate in the presence of an air leak but may lead to diffuse atelectasis, which cannot always be successfully counteracted by the background IMV. Different strategies aimed at obtaining optimal lung volume by the use of higher PEEP may be more appropriate when treating babies with respiratory distress syndrome in the absence of an air leak.

We conclude that HFJV allows the use of lower peak and mean airway pressures and leads to more frequent and more rapid improvement in PIE than does rapid-rate CV. Furthermore, HFJV is capable of rescuing moribund infants with air leaks in whom conventional therapy is failing and improves survival rates for such infants. The HFJV strategy used in this study did not increase the rate of complications. A trial of early use of HFJV in infants with respiratory distress syndrome for the purpose of preventing acute barotrauma and subsequent BPD is warranted.

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