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High-Frequency Jet Ventilation in Pediatric Acute Respiratory Failure

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Abstract

Background: High-frequency jet ventilation (HFJV) is primarily used in premature neonates; however, its use in pediatric patients with acute respiratory failure has been reported. The objective of this study is to evaluate HFJV use in the pediatric critical care setting. We hypothesized that HFJV would be associated with improvements in oxygenation and ventilation.

Methods: Medical records of all subjects who received HFJV in the pediatric intensive care unit (PICU) of a quaternary care center between 2014 and 2018 were retrospectively reviewed. Premature infants who not been discharged home were excluded as were those in whom HFJV was started while on ECMO. Data on demographics, pulmonary mechanics, gas exchange, and outcomes were extracted and analyzed using chi-squared testing for categorical variables, non-parametric testing for continuous variables, and a linear effects model to evaluate gas exchange over time.

Results: 35 subjects (median 2.9 months, 5.2 kg) were included. Prior to HFJV initiation, median oxygenation index (OI) was 11.3 (7.2-16.9), and P/F 133 (91.3-190.0), pH 7.18 (IQR: 7.11-7.27), $PaCO_2$ 64 (52-87) mmHg, PaO_2 74 (64-125) mmHg, For subjects still on HFJV (n=25)4-6 hours after initiation, there was no significant change in OI, P/F or PaO2 whereas pH increased (p=0.001) and $PaCO_2$ decreased (p=0.001). For those remaining on HFJV for over 72 hours (n=12), the linear effects model revealed no differences over 72 hours for OI, P/F, $PaCO_2$, or mPaw but there was a decrease in FiO_2, whereas pH and PaO_2 increased. There were no. Nine (26%) did not survive and non-survivors had higher PIM2 scores (p=0.01), were more likely to be immunocompromised (p=0.01), were less likely to have a documented infection (p=0.02), and had lower airway resistance (p=0.024).

Conclusions: HFJV was associated with improved ventilation among subjects able to remain on HFJV but had no significant effect on oxygenation.

Keywords: pediatric respiratory failure, high-frequency ventilation, jet ventilation, gas exchange, pediatric acute respiratory distress syndrome, mechanical ventilation, children, oxygenation, ventilation.

Introduction

Respiratory illnesses are the most common reason for admission to a pediatric intensive care unit (PICU).[1] A large, international, multi-center point prevalence study found 53% of patients required invasive or non-invasive ventilation.[2] The vast majority of children with acute respiratory failure requiring intubation and invasive support can be managed with conventional mechanical ventilation. Those with more severe or refractory respiratory failure, and in whom a lung protective strategy cannot be achieve through conventional ventilation, may be treated with high-frequency ventilation or extracorporeal life support (ECLS).[3] High-frequency modalities used within the PICU include high-frequency oscillatory (HFOV), high-frequency percussive ventilation (HFPV), and high-frequency jet ventilation (HFJV) although strong evidence supporting their use is lacking.[4] In the absence of guidance from high-quality data, individual centers currently elect to employ high frequency ventilation based on clinician preference, experience using each modality, and the patient's underlying physiology.

HFJV delivers high velocity inspiratory gas into the trachea through a jet injector. Inspiratory pulses are generated by flow stream interruption at a rate range between 240 and 660 cycles per minute with an inspiratory time of 0.02 to 0.03 seconds. This results in attenuation of the set peak inspiratory pressure (PIP) with a delivered tidal volume that is less than anatomic deadspace and theoretically avoids cyclic shearing stress observed during conventional ventilation.[5, 6] Peak inspiratory pressure during HFJV is controlled by the flow interrupter, but unlike HFOV, exhalation is passive.

HFJV is currently approved by the US Food and Drug Administration (FDA) for use in neonates up to 28 days of age, and it is used predominantly to treat perinatal respiratory failure in premature and term neonates admitted to a neonatal intensive care unit (NICU).[7-9] There are limited data evaluating

HFJV use outside of the NICU setting. Single center case series have shown successful use of HFJV in pediatric patients with air leak related to ARDS[10], critical bronchiolitis due to respiratory syncytial virus,[11] congenital diaphragmatic hernia[12] and pediatric ARDS (PARDS)[13], although some of these studies were conducted in the early 1990s and pre-date the wide-spread adoption of lung-protective ventilation. In addition, HFJV has been used in pediatric patients with congenital heart disease, with improved carbon dioxide (CO_2) clearance but minimal effect on oxygenation.[14, 15] Thus, there is a need for additional data evaluating HFJV in larger sample sizes and mixed patient population.

In our PICU, HFJV is used in the setting of inadequate gas exchange, refractory air leak, pulmonary interstitial emphysema, or inability to achieve lung-protective settings as defined by the Pediatric Acute Lung Injury Consensus Conference (PALICC) via a conventional ventilator.[4, 16] HFJV is generally our first choice of high-frequency ventilation in infants with oxygenation and ventilation failure while HFOV is used in patients with more severe oxygenation and ventilation failure or in larger patients in whom HFJV would likely be ineffective, although clinical practice varies depending upon each patient's pathophysiology. We conducted this study to demonstrate the feasibility of HFJV use in a cohort of critically ill infants with acute respiratory failure treated in the PICU. We hypothesized that HFJV would result in improvements in oxygenation and ventilation.

Methods

Following Institutional Review Board approval with waiver of informed consent, we reviewed the medical records of all subjects older than 14 days of age who received HFJV in our PICU between July 2013 and December 2018. Subjects were excluded if HFJV was started while the subject was on ECMO or in the NICU. Subjects were identified through a search of the electronic medical records. We collected demographic data, pertinent medical history, documented infection, surgical history, pre-HFJV ventilator settings, pre-HFJV arterial blood gas measurements, initial HFJV settings, dynamic compliance,

airway resistance, volume of exhaled carbon dioxide (VCO_2), need for ECLS or nitric oxide use, duration of HFJV support, and survival.

Dynamic compliance, airway resistance, and carbon dioxide elimination (VCO_2) measurements just prior to transition to HFJV were measured by an NM3 monitor (Phillips North America Corporation, Andover, MA). Oxygenation index (OI), PaO_2/FiO_2 ratio (P/F), and ventilation index were calculated from pre-HFJV values. The pre-HFJV mPaw used for calculations was the measured mPaw from the conventional ventilator, and post-HFJV initiation the documented mPaw was measured by the HFJV ventilator. During HFJV, a conventional ventilator operating in tandem with the HFJV ventilator is used to apply PEEP. The desired PEEP value is set on the conventional ventilator and is continuously measured by the HFJV ventilator. Pediatric Index of Mortality 2 (PIM2) score was calculated from PICU admission values. Ventilator and gas exchange data were extracted (when available) prior to HFJV initiation, at 4 to 6 hours, 24 hours, 48 hours, and 72 hours post-HFJV initiation, and when subjects were transitioned back to conventional mechanical ventilation.

Subjects were managed via a respiratory therapist (RT)-driven protocol for both conventional and HFJV. The primary conventional ventilator mode used in this protocol is pressure-SIMV. The protocol targets a tidal volume of 6-8 ml/kg for machine triggered breaths and 4-8 ml/kg for spontaneous breaths. PEEP is managed via a PEEP:FiO_2 table, peak inspiratory pressure is maintained ≤ 30 cm H_2O, and goal pH is ≥ 7.25. Inadequate gas exchange was defined in our conventional ventilator protocol as a pH < 7.25, inadequate oxygenation as per clinical discretion based on the subject's pathophysiology, or inability to maintain a lung protective strategy with peak inspiratory pressure ≤ 30 cm H_2O. For the HFJV protocol, mPaw is titrated to optimal lung inflation and oxygenation, HFJV rate is adjusted to minimize air-trapping as measured by the difference in set PEEP and PEEP measured by HFJV, conventional ventilator rate is set at 0-5 breaths per minute, and goal pH is > 7.25. Optimal lung inflation is defined as 8-9 ribs of expansion on bedside chest radiography. When initiating HFJV, the

mPaw is usually set equal to the mPaw on conventional ventilation. Details of both protocols are included in supplemental files A and B. HFJV was conducted with a Bunnell LifePulse ventilator (Bunnell Incorporated, Salt Lake City, UT) in tandem with an Avea ventilator (Vyaire, Yorba Linda, CA).

The primary physiologic outcome was change in oxygenation as defined by oxygenation index. Secondary outcomes included change in ventilation as measured by increase in pH with a decrease in $PaCO_2$, duration of mechanical ventilation, duration of HFJV support, need for ECMO or inhaled nitric oxide, survival, and need for oxygen supplementation at discharge. HFJV failure was defined as transition to another high-frequency mode or ECMO and data collection was discontinued. We chose not to include adverse events such as barotrauma as it was not possible to attribute adverse events to HFJV in a retrospective chart review.

Data were extracted from the medical records by trained RTs and entered into a REDCap database. OI was calculated as (mPaw x FiO_2 x 100)/PaO_2. Ventilation index was calculated as (respiratory rate x (peak inspiratory pressure – PEEP) x $PaCO_2$)/1000.

Continuous data are presented as medians and interquartile range, and categorical variables are presented as counts and percentages. We performed paired non-parametric analysis to evaluate the change in pH, $PaCO_2$, PaO_2, HCO_3, OI, and P/F between pre-HFJV values and at 4 to 6 hours post HFJV. The Wilcoxon Signed Ranked Test was performed to compare change in blood gas parameters, oxygenation index, and P/F 4-6 hours post HFJV initiation. To compare blood gas results, OI, P/F, and HFJV settings over time, separate linear mixed-effects models using exchangeable covariance structure were constructed. The following transformations for normal distribution were performed prior to model construction: OI, PF, PEEP, and mPaw by logarithmic function; $PaCO_2$, PaO_2, and HCO_3^- by inverse square root function; rate by square function; and FiO_2 by inverse function. For each model, subjects were included as random effects. Normality, homoscedasticity, and linearity assumptions were assessed by

visual inspection and plots of residuals against fitted values. Subgroup analysis of only those remaining on HFJV for more than 72 hours was performed to evaluate the effect of survivor bias. For survivors vs. non-survivors, continuous variables were compared using an independent samples Mann-Whitney U Test while categorical variables were compared using the chi-square test. Statistical significance was defined as a $p < 0.05$, and data were analyzed using SPSS v24 (Chicago, IL) and Stata 16.1 (College Station, TX).

Results

Forty subjects were placed on HFJV in the PICU during the time frame studied. Five subjects were excluded due to HFJV being initiated while on ECMO, so 35 subjects were included in the study with a median age of 2.9 (IQR: 1.6-7.9) months and weight of 5.2 (3.8-6.9) kg. Overall, 9 (26%) of subjects died. Subjects were on conventional ventilation for a median of 0.6 (0.1-2.9) days prior to HFJV. A total of 9 (26%) required ECMO, and 7 (77%) of those receiving ECMO survived. Respiratory failure was the primary indication for mechanical ventilation in 34 (97%) subjects with one subject receiving HFJV due to sepsis post-operatively. Infection was documented in 26 (74%) of subjects, with 22 (63%) having a viral infection. The most common viral infections noted were respiratory syncytial virus 14 (63%) and rhinovirus 8 (36%) (Table 1).

Blood gas analysis prior to HFJV initiation was not available in 5 subjects. Pre-HFJV measurements for the remaining 30 subjects had a median pH of 7.18 (7.11-7.27), $PaCO_2$ 64 (52-87) mmHg, PaO_2 74 (64-125) mmHg, HCO_3 26 (22-32) mEq/L, and base deficit -2 (-8-3) mmol/L. Complete data were available for calculated values in 27 subjects with a median OI 11.3 (7.2-16.9), PaO_2/FiO_2 133 (91.3-190.0), and ventilatory index 47 (35-64). Conventional ventilator settings prior to initiation of HFJV, available for 30 subjects, were a set respiratory frequency of 30 (28-34) breaths per minute, peak inspiratory pressure 30 (29-31) cm H_2O, set inspiratory pressure 22 (20-24) cm H_2O, set PEEP 8 (7-9) cm

H_2O, mPaw 14 (11-16) cm H_2O, and FiO_2 0.70 (0.50-1.00). Tidal volume was 5.6 (4.5-6.8) ml/kg, airway resistance 103 (78-156) cmH2O/L/s, and lung compliance was 2.1 (1.6-3.0) ml/cmH2O.

Ten of 35 (29%) subjects did not have a blood gas 4-6 hours after HFJV initiation. Of these, 3 were placed on ECMO, 3 transitioned to HFOV, 3 transitioned back to conventional mechanical ventilation, and 1 was placed on HFPV. For the 25 subjects with complete data at 4-6 hours after HFJV initiation, paired non-parametric analysis demonstrated no significant differences in OI (11.4 vs. 10.0, p=0.85), P/F (133 vs. 112.0, p=0.63), or PaO_2 (74 mmHg vs. 79 mmHg, p=0.39); however, pH increased (7.18 vs. 7.39, p=0.001), $PaCO_2$ decreased (64 mmHg vs. 51 mmHg, p=0.001), and HCO_3 increased (26 mEq/L vs. 29 mEq/L p=0.007). Linear effects model revealed that in subjects who remained on HFJV for 72 hours, HCO_3^- and HFJV rate significantly decreased, whereas pH, base excess/deficit, set PEEP, and FiO_2 significantly increased. Subgroup analysis of only those 12 subjects remaining on HFJV for more than 72 hours revealed similar results as the complete cohort (Table 2).

Eighteen (51%) subjects were ultimately transitioned from HFJV to conventional mechanical ventilation without ECMO or another high-frequency mode after a median time on HFJV of 5.4 (0.8-11.1) days. Three subjects were transitioned to conventional ventilation within 4-6 hours, five within 24 hours, 2 within 48 hours, and 1 within 72 hours with the remaining 9 being transitioned after more than 72 hours of HFJV. Of the 17 (49%) subjects who were unable to be transitioned back to conventional mechanical ventilation, 9 (53%) received ECMO, 5 (29%) HFOV, 1 (6%) HFPV, and 2 (12%) died while on HFJV. One subject transitioned successfully from HFJV but expired later. HFJV settings prior to transition to conventional ventilation were: PIP 39 (32-50) cm H_2O, mPaw 14 (11-17) cm H_2O, and FiO_2 0.50 (0.35-0.56). (Table 3). Conventional mechanical ventilation settings at transition from HFJV were set respiratory rate 30 (26-33) breaths per minutes, set inspiratory pressure 20 (16-23) cm H_2O, set PEEP 8 (6-10) cm H_2O, and FiO_2 0.45 (0.39-0.60).

Non-survivors had higher PIM2 scores (6.3% vs. 1.6%, p=0.01), were more likely to be immunocompromised (44% vs. 8%, p=0.01), were less likely to have a documented infection (44% vs. 85%, p=0.02), and had lower airway resistance (111 $cmH_2O/L/s$ vs. 66 $cmH_2O/L/s$, p=0.024). There were no differences for age, weight, initial OI, initial P/F ratio, ventilatory index, pH, $PaCO_2$, PaO_2, HCO_3, base excess/deficit, OI 4-6 hours post HFJV initiation, and P/F 4-6 hours post HFJV initiation (Table 4). There were no differences for time on MV prior to HFJV (p=0.78), total time on HFJV (p=0.12), reason for mechanical ventilation (p=0.56), history of congenital heart disease (p=0.43), prematurity (p=0.25), congenital syndromes (p=0.14), or prior surgery (p=0.75). There was no difference in the need for ECMO (p=0.78) or inhaled nitric oxide (p=0.21). There were no differences in conventional ventilator settings, observed mPaw, lung compliance, tidal volume, VCO_2, or initial HFJV settings. (Supplemental Table A).

Discussion

In this study, we describe our experience with HFJV in infants with acute respiratory failure from multiple etiologies. To our knowledge, this is the largest and most varied HFJV cohort in non-neonatal pediatric subjects. Short-term success was seen in 71% of subjects, with $PaCO_2$ and pH improved 4-6 hours post HFJV initiation and remaining stable for those remaining on HFJV over 72 hours. The improvement in gas exchange variables was likely overestimated as the 29% of subjects who failed HFJV would not have had improved gas exchange or potentially worsening gas exchange. While the PIP was much higher than during conventional ventilation, there is significant attenuation of PIP during HFJV throughout the respiratory system.[6] However, a total of 43% of subjects ultimately required transition to other high-frequency modalities or ECMO. There was no effect on OI or P/F observed at 4-6 hours or over 72 hours.

Survivors had a high rate of viral infection, predominantly RSV, underscoring that respiratory failure as the result of RSV has a better prognosis than other etiologies.[17] As expected, non-survivors had

a statistically significant higher illness severity as indicated by immunocompromised state and higher PIM2 scores; and trended toward a lower pH and lower base deficit, although these were not statistically significant. There were also no differences in oxygenation index, ventilation index, FiO_2, and set respiratory rate between survivors and non-survivors.

There is a paucity of data evaluating HFJV outside of the neonatal population, and most prior studies have focused on single-diseases states such as viral bronchiolitis. Valentine et al. described the use of HFJV in a series of 11 infants and children (1.7 to 14.2 kg, aged 2 weeks to 39 months) with respiratory syncytial virus. They observed increased pH and decreased $PaCO_2$, and a 91% (10/11) survival to discharge.[11] The majority (9/11) of their subjects were born prematurely, compared to only 26% in our cohort. Their median ventilation index was 55 and the OI was 14, higher than what was observed in our study. The median pH, $PaCO_2$, or PIM2 scores were not reported in that study. The differences in outcome between that study and ours are likely attributed to the etiology of acute respiratory failure; our study included subjects with undifferentiated acute respiratory failure from multiple etiologies, whereas theirs included only subjects with RSV, who are expected to have a high survival rate.[17, 18]

The change in gas exchange observed in our study is similar to those of Zhang et al., who described a series of 25 infants (mean weight 2.8 kg) with congenital diaphragmatic hernia (CDH) managed with HFJV. In that study, HFJV was associated with minimal complications and resulted in a significant increase in pH and decrease in $PaCO_2$ over an unreported timeframe, with a mortality rate of 64%.[12] Infants with CDH are also managed with HFJV in our center; however, they were not included in this study as they are managed within our NICU by a separate clinical team.[19] Smith et al. evaluated HFJV use in 29 pediatric subjects with PARDS complicated by air leak syndrome and found a survival rate of 64%.[10] In that study, survivors spent significantly less time on conventional ventilation prior to HFJV than non-survivors (3.7 days vs. 9.6 days) suggesting that early application of HFJV might be beneficial although this study was published in 1993 and subjects were receiving a PIP of 49 cmH_2O prior to HFJV.

Our clinical practice embraces this early HFJV strategy, as evidenced by our median time on CMV prior to HFJV of 0.6 days.

The clinically important improvement in ventilation observed in our study suggests that HFJV can be of value in patients with increased airway resistance, such as bronchiolitis, with significant respiratory acidosis that is refractory to conventional ventilation. HFJV can significantly decrease $PaCO_2$ and should be considered for patients in whom conventional ventilation requires an elevated plateau pressure, peak inspiratory pressure, and/or driving pressure for adequate ventilation. In our study, there may have been room to increase the set respiratory frequency as the median frequency was 30 breaths per minute; however, there was no way to assess if air-trapping and auto-PEEP were present prior to HFJV due to our methodology. In the future, it is possible that PaCO2 could be managed by increasing the respiratory frequency, inspiratory time, or adjusting PEEP to increase lung recruitment prior to transitioning to HFJV. Despite PEEP being increased following HFJV initiation, there were no statistically significant differences in PEEP or mPaw. There was no change in oxygenation at 4 to 6 hours, indicating that HFJV may not have a short-term impact on oxygenation, and while FiO_2 decreased over time, there were no differences for OI or P/F. The effect of HFJV on oxygenation may be related to minimal lung recruitment despite the higher PIP. Lung recruitment during HFJV can be achieved by increasing the PEEP or respiratory frequency on the conventional ventilator. PEEP set on the conventional ventilator is the primary driver of mPaw during HFJV, although higher HFJV rates are associated with increased air trapping, a strategy that may be counterproductive in patients with increased airway resistance, such as bronchiolitis. For patients with acute lung injury, our protocol calls for increasing the mPaw by 5-6 cmH_2O at initiation; however, there was no significant difference in mPaw after HFJV initiation.

While a randomized controlled trial of HFJV would be ideal, we feel this is likely unfeasible as HFJV is not widely used in PICUs. Future case series should focus on the feasibility of HFJV in larger patients and patient populations in which HFJV has not been extensively studied. These studies should

attempt to incorporate the use of advanced imaging techniques such as electric impedance tomography to evaluate the effect of HFJV on lung volumes.

This study has several limitations, including a small sample size. As a retrospective study, we were limited to the data that were available in the medical record. This was a single center study at an academic medical center with extensive experience using HFJV in its various neonatal and pediatric critical care units, and thus may not be generalizable to other centers. The lack of a control group limits the generalizability of the study and we were unable to evaluate a group that was not treated with HFJV. We did not record adverse events such as barotrauma as it was not possible to attribute adverse events to HFJV, high pre-HFJV ventilator settings or manual ventilation with high pressure due to our methodology. The PIM2 score may not be predictive of mortality risk in a cohort of children predominantly admitted for viral respiratory failure.[20] There was potential selection bias by the clinical team when initiating HFJV. The plateau pressure was not documented; and, therefore, driving pressure could not be determined. We were unable to perform multivariable analyses or sub group analyses to further delineate various associations due to our limited sample size. Only three subjects were greater than 10 kg (with 2 being 10.1 and 10.4 kg) so we were unable to evaluate if there was an upper weight limit to HFJV.

Conclusion

In subjects who remained on HFJV 4-6 hours after initiation, HFJV was associated with improved ventilation but no significant change in oxygenation. HFJV was moderately successful with many subjects requiring other high-frequency modes or ECMO.

Quick Look

Current Knowledge:

Children with severe respiratory failure are currently treated with high-frequency ventilation. High-frequency jet ventilation (HFJV) is primarily used in premature neonates; however, its use in pediatric patients with acute respiratory failure has been reported in small single center case series in a variety of patient populations. In our PICU, HFJV is used in the setting of inadequate gas exchange, refractory air leak, pulmonary interstitial emphysema, or inability to achieve lung-protective settings via conventional ventilator. We conducted this study to demonstrate the feasibility of HFJV use in a cohort of critically ill infants (median age 2.9 months) with acute respiratory failure treated in the PICU.

What this paper contributes to our knowledge

HFJV in pediatric acute respiratory failure was feasible in severe respiratory failure resulting from multiple etiologies. In subjects with a median weight of 5.2 (3.8-6.9) kg, there were short-term improvements in $PaCO_2$ and pH in 71% of subjects and ventilation remained stable over 72 hours. There were no significant changes in oxygenation at 4-6 hours post initiation or over 72 hours. A total of 43% of subjects required transition to other high-frequency modalities or ECMO and overall survival was 74%.

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Table 1 – Patient Characteristics	
Characteristic	**Median (IQR) or n (%) (N = 35)**
Weight, kg	5.2 (3.8-6.9)
Age, months	2.9 (1.6-7.9)
PIM2, %	2.1 (1.0-6.2)
Reason for MV	
Respiratory failure	34 (97.1%)
Post-operative	1 (2.9%)
Co-morbidities	
Prematurity	9 (26%)
Chronic lung disease	9 (26%)
Immunocompromised	6 (17%)
Congenital syndromes	6 (17%)
Congenital heart disease	5 (14%)
Prior surgery	5 (14%)
Laboratory-proven infection	
Bacterial	4 (11%)
Viral+	22 (63%)
RSV	14 (64%)
Rhinovirus	8 (36%)
Parainfluenza	2 (9%)
Adenovirus	1 (4.5%)
Enterovirus	1 (4.5%)
CMV	1 (4.5%)
None	9 (26%)
Surgical history	
None	27 (77%)
Abdominal surgery	3 (9%)
Gastric tube	3 (9%)
Cardiac surgery	1 (3%)
Other	1 (3%)
Outcomes	
Survived	26 (74%)
ECMO	9 (26%)
Inhaled Nitric Oxide	12 (34%)
Time on MV pre-HFJV, days	0.6 (0.1-2.9)
Total time on HFJV, days (n=18)*	5.4 (0.8-11.1)

+ Three subjects tested positive for multiple viruses.

** For those transitioned back to conventional ventilation; excludes patients who died, required ECMO, or were transitioned to another high-frequency mode.*

Continuous variables presented as median (IQR); categorical variables presented as count (percent)

CMV, cytomegalovirus; ECMO, extracorporeal membrane oxygenation; HFJV, high-frequency jet ventilation; MV, mechanical ventilation; PIM2, Pediatric Index of Mortality; RSV, respiratory syncytial virus

Flow Chart of Subjects in the Study

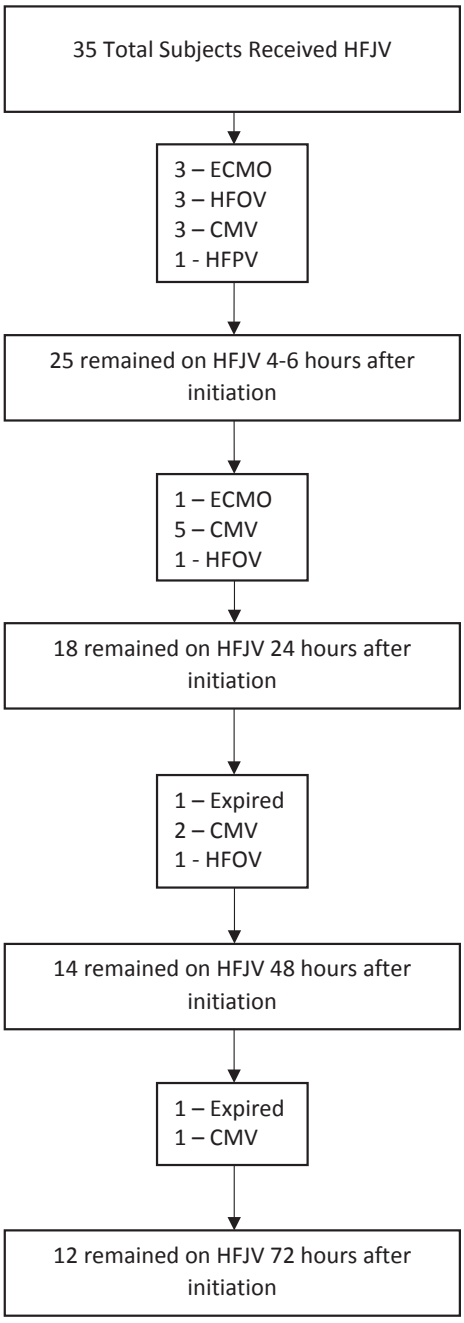

Figure Legend: HFJV = high-frequency jet ventilation, CMV=conventional mechanical ventilation, HFOV = high-frequency oscillatory ventilation, HFPV = high-frequency percussive ventilation

Table 2 – Change in HFJV Oxygenation and Ventilation Variables Over Time

Variable	Pre-HFJV	4-6 hours	24 hours	48 hours	72 hours	Linear Mixed Model++	
						β	p-Value
Subjects	30	25	18	14	12		
OI	11.4 (7.2-16.9)+	10.0 (8.2-16.6)	11.7 (8.5-15.7)	9 (6.4-15.5)	8.5 (6.3-11.6)	-2.25×10^{-3}	0.33
P/F	133.3 (91.3-190.0)+	112 (72.6-176.1)	138 (93.8-162.5)	145.3 (108.2-230.4)	138.0 (118.0-181.9)	1.54×10^{-3}	0.49
Arterial blood gas							
pH	7.18 (7.11-7.27)	7.39 (7.25-7.43)*	7.38 (7.32-7.42)	7.41 (7.37-7.46)	7.39 (7.36-7.44)	2.54×10^{-3}	**<0.001**
$PaCO_2$, mmHg	64 (52-87)	51 (42-60)*	50 (45-58)	51 (42-63)	54 (46-70)	1.28×10^{-4}	0.10
PaO_2, mmHg	74 (64-125)	79 (58-105)	76 (69-94)	87 (67-115)	76 (69-88)	-9.61×10^{-6}	0.91
HCO_3^-, mEq/L	26 (22-32)	29 (22-32)*	28 (25-33)	31 (28-36)	34 (31-41)	-4.08×10^{-4}	**<0.001**
Base excess/deficit, mmol/L	-2 (-8-3)	4 (-4-6)	4 (-1-6)	7 (3-9)	9 (6-12)	0.11	**<0.001**
HFJV Settings	**Initial HFJV**						
PIP, cm H_2O	46 (40-50)	45 (40-49)	44 (38-47)	44 (41-44)	43 (38-48)	-9.23×10^{-3}	0.70
Rate, breaths/min	360 (320-420)	360 (320-380)	360 (320-390)	320 (300-360)	320 (300-360)	-285.4	**0.04**
Ti, sec	0.02 (0.02-0.03)	0.02 (0.02-0.03)	0.03 (0.02-0.03)	0.03 (0.02-0.03)	0.03 (0.02-0.03)	-1.50×10^{-4}	0.37
Set PEEP, cm H_2O	8 (7-9)	10 (8-12)	10 (10-12)	10 (10-11)	11 (9-12)	3.58×10^{-3}	**0.002**
FiO_2	1.0 (0.60-1.00)	0.65 (0.50-0.90)	0.57 (0.50-0.63)	0.58 (0.45-0.70)	0.50 (0.46-0.65)	7.74×10^{-3}	**<0.001**
mPaw, cm H_2O	14 (11-16)	13.9 (11.8-17.0)	15.8 (12.3-17.2)	14.5 (12.0-16.9)	15.5 (11-17.6)	2.11×10^{-4}	0.87

** p < 0.05 compared to pre-HFJV*

+ Available for 27 subjects

++ Select variables transformed for normality: OI, P/F, PEEP, and mPaw by logarithmic; $PaCO_2$ PaO_2, and HCO_3^- by inverse square root; rate by square; and FiO2 by inverse

Continuous variables presented as median (IQR); categorical variables presented as count (percent)

β, *slope; FiO_2, fraction of inspired oxygen; H_2O, water; HCO_3^-, bicarbonate; HFJV, high-frequency jet ventilation; mPaw, mean airway pressure; OI, oxygenation index; P/F, PaO_2:FiO_2 ratio; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; Ti, inspiratory time*

Table 3 – Post-HFJV Oxygenation and Ventilation Variables	
Variable	**Median (IQR) or n (%) (N = 18)**
Final HFJV settings	
PIP, cm H_2O	39 (32-50)
mPaw, cm H_2O	14 (11.0-16.5)
FiO_2	0.50 (0.35-0.56)
Conventional MV settings	
Set respiratory rate, breaths/min	30 (26-33)
Set inspiratory pressure, cm H_2O	20 (16-23)
Set PEEP, cm H_2O	8 (6-10)
FiO_2	0.45 (0.39-0.60)
mPaw, cm H_2O	13 (11-15.5)
Compliance, ml/cm H_2O	3 (1.9-3.6)
Vt, ml/kg	7.0 (5.4-8.0)
Airway resistance, cm H_2O/L/s	106 (78.5-172.0)
VCO_2, ml/min	26.6 (19.6-32.3)
Post transition to conventional MV blood gas	
pH	7.33 (7.29-7.42)
$PaCO_2$, mmHg	53 (42-64)
PaO_2, mmHg	75 (69.0-111.5)
HCO_3^-, mEq/L	29 (24.5-31.5)
Base excess/deficit, mmol/L	3 (-1-5)
Post transition calculated values	
OI	6.7 (4.4-12.1)
P/F	192.5 (125.0-308.6)
Ventilatory index	27.1 (17.7-45.8)

Continuous variables presented as median (IQR); categorical variables presented as count (percent)
FiO_2, fraction of inspired oxygen; H_2O, water; HCO_3^-, bicarbonate; HFJV, high-frequency jet ventilation; mPaw, mean airway pressure; OI, oxygenation index; P/F, PaO_2:FiO_2 ratio; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; VCO_2, volume of exhaled carbon dioxide; Vt, tidal volume

Table 4 – Comparison of Survivors vs. Non-Survivors					
Variable	**N**	**Survivors**	**N**	**Non-Survivors**	**P-Value**
Subjects		26 (74%)		9 (26%)	
Demographics					
Age, months	26	2.7 (1.7-7.6)	9	6.8 (0.4-10.1)	0.87
Weight, kg	26	5.2 (3.8-6.8)	9	5.2 (3.4-8.7)	0.93
PIM2, %	26	1.6 (0.5-4.1)	9	6.3 (2.6-26.5)	0.01
Documented infection, Y (%)	26	22 (85%)	9	4 (44%)	0.02
Documented infection					
Bacterial	26	2 (8%)	9	2 (22%)	0.02
None	26	4 (15%)	9	5 (56%)	
Viral	26	20 (77%)	9	2 (22%)	
Calculated gas exchange variables					
Pre-HFJV OI	21	11.3 (7.5-16.9)	6	13.1 (6.5-15.9)	0.11
Pre-HFJV P/F	21	134.0 (71.5-198.8)	6	123.9 (97.8-205.5)	0.93
Ventilatory index	20	46.9 (34.0-55.2)	7	60.8 (39.3-70.2)	0.31
Arterial blood gas					
pH	23	7.22 (7.14-7.30)	8	7.13 (7.02-7.22)	0.054
$PaCO_2$, mmHg	23	64 (53-83)	7	68 (46-94)	>0.99
PaO_2, mmHg	23	72 (59-109)	7	86 (72-126)	0.47
HCO_3^-, mEq/L	23	27 (23-32)	7	18 (13-31)	0.054
Base excess/deficit, mmol/L	23	-1 (-5-4)	7	-10 (-12-1)	0.061
OI 4-6 hours post HFJV	19	10 (8.1-16.7)	5	9.9 (6.6-29.8)	0.73
P/F 4-6 hours post HFJV	19	118.6 (78.6-164)	6	93.1 (33.8-246.2)	0.56

Continuous variables presented as median (IQR); categorical variables presented as count (percent)
HCO_3^-, bicarbonate; HFJV, high-frequency jet ventilation; OI, oxygenation index; P/F, PaO_2:FiO_2 ratio; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; PIM2, Pediatric Index of Mortality