Journal of Perinatology (2007), 1–5

www.nature.com/jp

ORIGINAL ARTICLE

Safety and efficacy of high-frequency jet ventilation in neonatal transport

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Objective: To evaluate the safety and efficacy of high-frequency jet ventilation for transporting critically ill hypoxic neonates to an extracorporeal membrane oxygenation (ECMO) center.

Study Design: We conducted a retrospective cohort study of 38 transported neonates. Safety was assessed by the comparison of cardiopulmonary variables before and after transport from referring hospital to our ECMO unit. Efficacy was assessed as the effect on ventilation and efficiency of pulmonary gas exchange after conversion from a conventional mechanical ventilator or a high-frequency oscillator to a high-frequency jet ventilator±inhaled nitric oxide.

Result: The pre- and posttransport vital signs remained stable, regardless of the type of ventilator used. Pre-transport pneumothorax was the main problem, but no transport-related deaths occurred. We found significant improvement in the ventilation of the neonates transported with a high frequency jet ventilation±inhaled nitric oxide that were deficient in those transported with conventional mechanical ventilation + inhaled nitric oxide ($P<0.05$). The improvement started before transport upon changing the mode of ventilation to a high-frequency jet ventilator.

Conclusion: Independent of the use of inhaled nitric oxide, high frequency jet ventilation appears to provide better ventilation than conventional mechanical ventilation and is safe to transport pre-ECMO neonates.
Journal of Perinatology advance online publication, 16 August 2007; doi:10.1038/sj.jp.7211799

Keywords: safety of HFJV; efficacy of HFJV; ECMO; inhaled nitric oxide; neonatal transport

Introduction

Inter-facility neonatal transport became an integral part of medical care after state-based, regionalized systems of perinatal care were established in North America almost three decades ago.[1] With the dissemination of advanced technologies into the neonatal community, the personnel of centers providing extracorporeal membrane oxygenation (ECMO) have found themselves transporting very critically ill neonates from units that have already initiated sophisticated levels of treatment, such as high-frequency ventilator and inhaled nitric oxide (iNO). Although maintaining sophisticated levels of support during transport is challenging, critically ill neonates are being transported with increasing frequency on full ventilation support with either conventional mechanical or high-frequency ventilators including the administration of iNO.

After US Food and Drug Administration (FDA) approval, the use of iNO in conjunction with a high-frequency ventilator to facilitate oxygenation in severely hypoxic neonates was accelerated.[2] The use of iNO or a high-frequency ventilator has been shown to decrease the need for ECMO,[3–5] but consequently, also increases the need to promptly transport nonresponders with the same combination of high-frequency ventilation and iNO to an ECMO center.

Two studies have reported transporting a neonate on a Drager or Infant Star conventional mechanical ventilator with iNO,[4,6] while another reported the transport of pre-ECMO neonates with manual pressure ventilation (Neopuff by Fisher & Paykel, Panmure, New Zealand)±iNO.[7] Comparative neonatal ventilator studies have been done within neonatal intensive care units (NICUs),[8,9] but there are no comparative studies using different kinds of ventilators with iNO during transport. Our retrospective study compared the safety and efficacy of using a conventional mechanical ventilation (CMV) vs using a high-frequency jet ventilation (HFJV) with or without iNO during transport.

Methods

To evaluate the safety and efficacy of HFJV for the transport of critically ill pre-ECMO neonates, we conducted a retrospective cohort study of neonates referred to us for ECMO because of severe acute respiratory failure for the years 1998 to 2004. We defined severe acute respiratory failure as any intubated and mechanically supported neonate with or without iNO and/or an oxygenation

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Received 19 December 2006; revised 8 May 2007; accepted 13 June 2007

index (OI) of ⩾10, an average value that triggers the majority of sending physicians to initiating transfer to our ECMO facility (data not shown). Our transport team consisted of a fellow (pediatrician in training to be a neonatologist), one or two trained registered transport nurses and a respiratory therapist in an ambulance designed specifically for neonatal transport. After approval of the study by the Institutional Review Board, the charts of 38 neonates were reviewed. We tabulated patients' demographic data and transport time (recorded length of time taken by the transport team upon leaving the referring hospital up to the time of arrival in our unit).

Safety and efficacy were compared for neonates who were transported using CMV + iNO vs those with HFJV ± iNO. Before FDA approval in December 1999 (13 patients), iNO was used as an investigator-initiated investigational new drug exemption approved by our institutional review board. An Airborne brand portable transport incubator (International Biomedical, Austin, TX, USA) was used for all transport and modified to accommodate HFJV within this system. The iNO was blended into the constantly flowing gas and delivered through the inspiratory limb of the CMV portion of the HFJV system that was connected with the iNOvent device (Datex-Ohmeda, Madison, WI, USA) to provide HFJV, or before FDA approval of iNOvent, to an AeroNOx device (Pulmonox Medical Inc., Alberta, CA, USA). The HFJV was connected directly to the distal end of the endotracheal tube (ET) (Figure 1).
We evaluated the following measures of safety: (1) cardiopulmonary variables: vital signs (heart rate, mean arterial pressure), partial pressure of CO_2 (P_aCO_2) as a measure of the effectiveness of ventilation and OI as a measurement of pulmonary gas exchange: $((P_{aw} \times FiO_2 \times 100)/P_aO_2)$, mean airway pressure ($P_{aw}$) as an estimate of ventilator support and arterial blood pH, (2) the frequency of problems or complications such as ET dislodgment, loss of 'chest wiggle' (signifying equal and continuous chest vibration by high-frequency ventilation as a visual evidence of optimum placement of ET tube) and pulmonary leak, (3) the need for ECMO within 48 h of arrival and stability to be discharged or transferred back to the referral unit or death. The efficacy was evaluated as the improvement of the above cardiopulmonary variables after ventilator change from CMV or high-frequency oscillatory ventilator (HFOV) to HFJV before transport. The transport team under the direction of the attending neonatologist determined the need to change from CMV to HFJV before transport. All the variables were recorded before and after changing the ventilator or shortly before the team's departure from the referring hospital and upon arrival and stabilization of the neonates in our NICU.

Statistical analysis

Data recorded as before and after were analyzed by repeated measures two-way analysis of variance and, if significant, groups were compared by Holm–Sidak test. Other categorical variables were compared by Wilcoxon signed-rank test and continuous variables by *t*-test. Significance was defined as $P \leqslant 0.05$.
All values are expressed as mean ± standard error of means (s.e.m.).

Results

In a 7-year span, 38 neonates with severe acute respiratory failure potentially needing ECMO were transported from other hospitals to our unit. Majority of the transported neonates were supported by

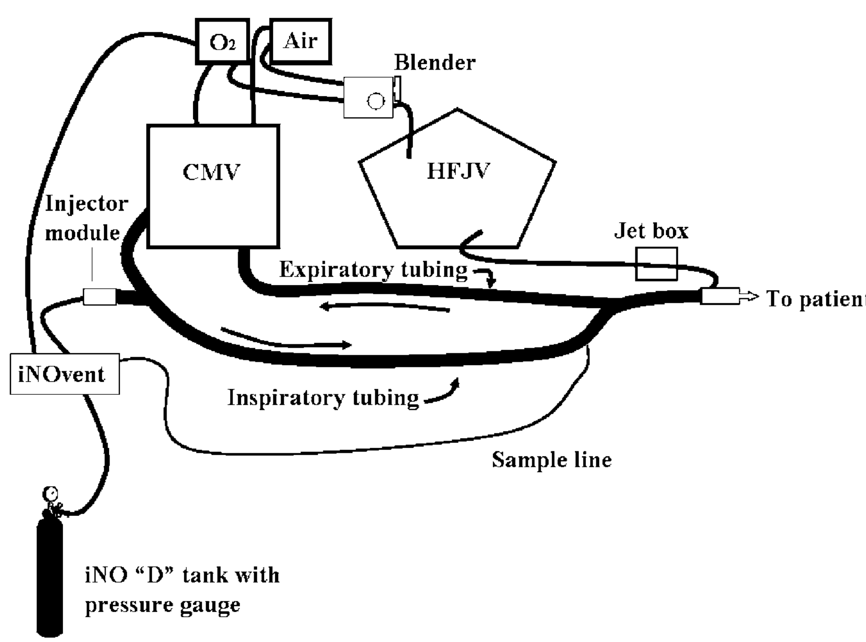

Figure 1 Schematic diagram of ventilators and iNO connected to the transported neonate.

HFJV with or without supplemental iNO and the rest by CMV with iNO. Based on the clinical condition of the patient, the supervising neonatologist decided before transport, to either change ventilation support from CMV to HFJV±iNO or remain with a CMV + iNO, while all neonates on HFOV were changed to HFJV. There were no significant differences in gender, gestational age, birth weight or transport time between transported neonates supported with a CMV + iNO and an HFJV±iNO. All neonates were term or near-term with birth weight ranging from appropriate to large for the gestation period. A majority of the transported neonates traveled more than 1 h (Table 1).

The neonates who were transported with HFJV, regardless of iNO supplementation, showed marked improvement in their ventilation (P_aCO_2) (Table 2, row 5) upon arrival in our unit, without augmentation of their ventilatory support. The reverse was true for those neonates transported with CMV. A similar trend was observed in the improvement of gas exchange (OI) and oxygenation in those transported with HFJV, but not those transported with CMV (rows 4 and 6). In all groups, the transported neonates maintained similar heart rates (row 1) and blood pressure (row 2).

We further investigated the significance of the improvement shown by groups supported by HFJV. Twenty-nine neonates transported on HFJV were changed from CMV or HFOV to HFJV at the referring hospital before transport. Regardless of iNO supplementation, there was a significant immediate improvement in ventilation (P_aCO_2) in all of these neonates (Table 3, row 5). Additionally, after changing to HFJV, the group that received iNO showed the ability to be ventilated with significantly lower

Table 1 Demographics of patients transported to the NICU (1998–2004)

	CMV with iNO (n = *9*)	*HFJV*	
		With iNO (n = *17*)	*Without iNO* (n = *12*)
Gender			
Male	5	11	6
Female	4	6	6
Gestational age (weeks)			
<37	0	2	2
>37	9	15	10
Weight (g)	3105–4275	2814–5495	2592–5100
Transport time (min)			
0–60	3	6[a]	1
61–170	6	10	11

Abbreviations: CMV, conventional mechanical ventilation; HFJV, high-frequency jet ventilation; iNO, inhaled nitric oxide.
[a]Transport time information is missing for one patient on HFJV+iNO.

Table 3 Effect of changing ventilator to the cardiorespiratory variables before transport

	CMV or HFOV to HFJV pretransport (mean ±s.e.m.) n = *29*			
	I. iNO (n = *17)*		*II. No iNO* (n = *12)*	
	CMV/HFOV	*HFJV*	*CMV/HFOV*	*HFJV*
1. HR (b.p.m.)	169±4	162±4	155±5	151±5
2. MAP (mm Hg)	52±2	49±2	53±3	43±3
3. P_{aw} (cm H_2O)	17±0.9	14±0.9[a]	12±1[b]	11±1[b]
4. PaO_2 (mm Hg)	115±21	122±21	125±25	201±25
5. $PaCO_2$ (mm Hg)	43±3	34±3[a]	49±3	40±3[a]
6. OI	29±3	20±3	16±4[b]	10±3[a,b]
7. pH	7.41±0.03	7.46±0.03	7.30±0.04	7.39±0.04[a]

Abbreviations: CMV, conventional mechanical ventilation; HFJV, high-frequency jet ventilation; HFOV, high-frequency oscillatory ventilator; HR, heart rate; iNO, inhaled nitric oxide; MAP, mean arterial pressure; OI, oxygenation index; P_{aw}, mean airway pressure; $PaCO_2$, partial pressure of CO_2; PaO_2, partial pressure of O_2.
[a]Significant difference between the values of before and after ventilator change.
[b]Significant difference between the values of the group receiving vs not receiving iNO.

Table 2 The cardiorespiratory variables of infants pre- and posttransport

Mean ±s.e.m.	*I. CMV+iNO* (n = *9)*		*II. HFJV+iNO* (n = *17)*		*III. HFJV* (n = *12)*	
Variables	*Pre*	*Post*	*Pre*	*post*	*pre*	*post*
1. HR (b.p.m.)	156±3	159±3	162±2	157±2	151±3	152±3
2. MAP (mm Hg)	63±2	53±2[a]	49±2	46±2	41±2	44±2
3. P_{aw} (cm H_2O)	13±0.5	13±0.5	14±0.2	14±0.8	11±0.4	12±0.4
4. PaO_2 (mm Hg)	151±21	102±21	112±15	129±15	201±18	206±18
5. $PaCO_2$ (mm Hg)	28±4	39±4	35±3	28±3[a]	40±3	32±3[a]
6. OI	16±4	22±4	21±3	13±3	10±3	7±3
7. pH	7.52±0.03	7.42±0.03[a]	7.45±0.02	7.47±0.02	7.39±0.02	7.48±0.02[a]

Abbreviations: CMV, conventional mechanical ventilation; HFJV, high-frequency jet ventilation; HR, heart rate; iNO, inhaled nitric oxide; MAP, mean arterial pressure; OI, oxygenation index; P_{aw}, mean airway pressure; $PaCO_2$, partial pressure of CO_2; PaO_2, partial pressure of O_2.
[a]Significant difference between pre- and posttransport values.

ventilator pressure (P_{aw}) than those without (row 3). The group of neonates who were receiving iNO before the change (column I) were sicker than those not receiving iNO before the change (Column II), as evidenced by the need for significantly higher ventilator pressure (row 3, 17 vs 12) and being less effective in gas exchange, OI (row 6, 29 vs 16). All patients were able to maintain blood acid–base balance as reflected by normal blood pH (row 7), either before and after changing the ventilator in the referring hospital (Table 3) or pre- and posttransporting the neonate to our unit (Table 2). The statistically significant increase or decrease in pH values was clinically irrelevant because the values were all within normal values.

There was no significant difference in the incidence of complications of patients transported with CMV or HFJV (Table 4). Most pneumothoraces occurred before transport rather than during or immediately after transport and there were no pneumothoraces-related fatalities. The three neonates who developed pneumothoraces during or immediately after transport received HFJV. Only one patient experienced ET dislodgment. As an indication of adequate ventilation, all of our transported patients on the HFJV maintained chest wiggle (Table 4).

The majority of the neonates went on to require ECMO after 48 h of their admission to our unit. With the exception of the three neonates who expired within 48 h of transport, all of them were either discharged home or sent back to the referring hospital (Table 5).

Discussion

The combination of high-frequency ventilation and iNO decreases the need for ECMO in most neonates with severe acute respiratory failure.[10,11] However, some neonates fail to respond to high-frequency ventilation and/or iNO, and since ECMO is not available in all centers, this leads to the daunting task of transporting them to an ECMO center. We are one of two centers in Virginia state that offer ECMO to the approximately 100 000 births that occur each year. In this study, the majority of our patients were transported within 2 h. Their heart rates and blood pressures were maintained within acceptable ranges during the transport, while pulmonary function and ventilation did not worsen and in some even improved. Other centers with experience transporting very ill neonates on CMV with or without iNO reported similar measures of safety as we report here.[6,12]

All neonates transported with HFJV with or without iNO supplement experienced significant improvement in ventilation and trended toward improvement in the effectiveness in gas exchange as measured by OI upon arrival in our unit, without the need to increase ventilator support. In contrast, those who were transported with CMV + iNO worsened slightly (Table 2). Since this study is a retrospective analysis, there was no randomized assignment of ventilators (CMV or HFJV). This potential selection bias was mitigated by the fact that the sickest infants were placed on HFJV and yet it was these neonates that experienced a marked improvement.

Despite an apparent improvement in patients ventilated with HFJV, either upon changing the ventilator at the referring hospital or after arrival in our unit, HFJV failed to show significant superiority on oxygenation over the other methods of ventilation. This may be due to the fact that the sicker neonates were the ones supported with HFJV or due to the small sample size.

We further investigated the group whose ventilation support was changed from CMV or HFOV to HFJV at the referring hospital. As shown in Table 3, ventilation improved with significantly lower ventilation support. These findings corroborate previous findings of the usefulness of HFJV as a rescue modality for neonates with respiratory failure supported by CMV.[13] Likewise, HFJV has also been found to be very effective in improving oxygenation and ventilation of in pre-ECMO neonates.[5]

While HFJV appeared to be better at improving oxygenation and efficiency in gas exchanges than the use of CMV, either immediately after changing ventilator to an HFJV (Table 3) or after the transported neonates reached our unit (Table 2), the values did not reach statistical significance. The iNO-to-CMV connection in our setup instead of the iNO-to-HFJV depends on the ability of the jet flow to entrain gas from the conventional limb. Platt *et al*.[14] have suggested that connecting the iNO to the jet limb may be more efficient and consistent and this might have affected the oxygenation.

Table 4 Transport-related complications

	I. CMV+iNO (n = 9)	*II. HFJV+iNO (n = 17)*	*III. HFJV (n = 12)*
Pneumothorax			
Before transport	1	3	4
After transport	0	2	1
ET dislodgment	1	0	0
Loss of 'chest wiggle'	NA	0	0

Abbreviations: CMV, conventional mechanical ventilation; ET, endotracheal tube; HFJV, high-frequency jet ventilation; iNO, inhaled nitric oxide; NA, not applicable.

Table 5 Outcomes

	I. CMV+iNO (n = 9)	*II. HFJV+iNO (n = 17)*	*III. HFJV (n = 12)*
ECMO within 48 h	2	3	1
Discharge home or transferred back to referring hospital	8	16	11
Expired within 48 h of admission	1	1	1

Abbreviations: CMV, conventional mechanical ventilation; ECMO, extracorporeal membrane oxygenation; HFJV, high-frequency jet ventilation; iNO, inhaled nitric oxide.

Pneumothoraces dominated the complications in our study population, but the majority of cases occurred before transport. Indeed, the decision to change from CMV or HFOV to HFJV before transport was often due to the recognition of the ability of HFJV to achieve acceptable oxygenation and ventilation at lower pressures in the presence of an air leak.[9,15] None of the neonates with continuing air leak was unstable during the transport. We acknowledge the limited ability of our retrospective study to discuss minor or rare complications or adverse events during transport.

Our study shows that ground transportation of critically ill neonates with severe acute respiratory failure with either CMV + iNO or HFJV ± iNO was safe for up to 170 min, as there were no significant transport-related complications. Our data indicate that HFJV ± iNO may be the preferred method of support for this subset of transported neonates due to its ability to optimize ventilation. Most of the neonates survived and were either discharged home or transferred back to the referring hospitals. In our experience, an HFJV with or without iNO is safe, efficacious and, indeed, preferred in transporting pre-ECMO neonates. Clearly, a prospective randomized controlled, multicenter study would be needed to affirm these findings.

Acknowledgments

We thank Gail Barker for assisting in data collection and Dr Shirley K DeSimone for editing and critical reading of the manuscript.

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