RESEARCH BRIEF

Rescue High Frequency Oscillation in Neonates with Acute Respiratory Failure

PREETHAM KUMAR PODDUTOOR , DINESH KUMAR CHIRLA, KAPIL SACHANE, FARHAN A R SHAIK AND ALLA VENKATLAKSHMI

From Rainbow Children's Hospital and Perinatal Centre, Banjara Hills, Hyderabad, India.

Correspondence to:
Dr Preetham Kumar,
Rainbow Children's Hospital,
Hyderabad 500 034, India.
drpreethamp@gmail.com
Received: June 6, 2010;
Initial review: July 14, 2010;
Accepted: October 28, 2010.

The aim was to study the efficacy of rescue High Frequency Oscillatory Ventilation (HFOV) in improving the oxygenation and ventilation in neonates with acute respiratory failure after failing Conventional Mechanical Ventilation (CMV). Primary outcome was short term oxygenation, lung recruitment, and ventilation and secondary outcome studied was survival. 675 babies were ventilated and 97 of them received HFOV. HFOV significantly improved oxygenation index, alveolar-arterial oxygen gradient, pH, PCO_2, PO_2 and caused better lung recruitment within 2 hours. Fifty seven babies (58.77%) survived and the mortality was more in <28 weeks, babies with pulmonary hemorrhage, sepsis and CDH.

Key words: *Failed CMV, High Frequency Oscillatory Ventilation, Rescue ventilation.*

Published online: 2011 February, 28. PII: S09747559INPE1000019-2

Pulmonary disease is a major cause of mortality and morbidity in term and near term infants. Conventional mechanical ventilation (CMV) has been used for many years but may lead to lung injury, require the subsequent use of more invasive treatment such as extracorporeal membrane oxygenation (ECMO), or result in death [1]. High frequency oscillatory ventilation (HFOV) is a new mode of ventilation using lung protective strategy [2] and the safer use of mean airway pressure that is higher than that generally used during CMV [3]. Studies suggest that HFOV is a better rescue therapy and also decreases the requirement of ECMO [4,5].

HFOV is being used in our unit for the past five years for various neonates with respiratory failure. As there are very few rescue studies reported, we intended to see the efficacy of HFOV in improving oxygenation and ventilation in babies who failed CMV.

METHODS

The study was a prospective observational study conducted from January 2006 to June 2009 at Rainbow Children's Hospital, Hyderabad, a 40 bedded tertiary level NICU. During the study period, 675 babies were ventilated, out of which 97 babies who required oscillation as per the unit protocol were included in the study.

Each baby with impending respiratory failure was ventilated conventionally and if the baby did not improve or deteriorated the following measures were done. Recruitment of the lung was prioritized by increasing the PEEP to a higher level of 7, followed by arterial blood gas (ABG) and a chest *X*-ray. If the *X*-ray showed under-inflation, then PEEP was increased to higher levels. Surfactant was given wherever necessary. On HFOV these babies were started on a MAP of 2 cm higher than the MAP on conventional ventilator and MAP was increased until a saturation of >95% was achieved (after which

priority was given to wean off FiO_2). The amplitude was adjusted based on the chest wriggle; frequency was started at 12Hz for the preterm babies and at 10 Hz for term babies and adjusted later based on ABG analysis. Recruitment of the lung was emphasized upon and reconfirmation of recruitment was done after 1-2 hours with chest radiograph (by two independent physicians). The baby was kept on the available oscillator Sensormedix 3100 A, SLE 5000 and Drager Babylog 8000 plus and rest of the treatment was given as per the standard unit protocols.

Criteria for starting HFOV: The criteria for starting HFOV were high pressures on CMV, inadequate oxygenation, ventilation, inadequate recruitment inspite of high PEEP, deterioration on CMV inspite of high pressures, and severe PPHN. Neonates who were referred from other hospitals after failing CMV and/or were unstable on CMV were directly put on HFOV.

Outcome measures: The ventilatory settings, ABG analysis (done as soon as possible after HFOV but in few instances took upto 2 hours), Oxygenation index (OI), Alveolar-arterial Oxygen Gradient ($AaDO_2$), duration of ventilation, and complications of ventilation were recorded during CMV and subsequently when shifted over to HFOV. Primary outcome was short term oxygenation, lung recruitment, and ventilation, and secondary outcome studied was survival.

Definitions: Adequate oxygenation PaO_2 50-80 mmHg; Appropriate ventilation: PCO_2 levels of 35-55 mmHg in preterm babies <7 days, in term babies and, preterm babies >1 week 40-60 mmHg; High pressures: PIP >25 mmHg in all babies or MAP >10 in preterm babies with FiO_2 requirement >0.5; Severe PPHN: OI >25 or Echocardiographic evidence of Suprasystemic pulmonary pressures; Appropriate recruitment: Lung volumes on *X*-rays >7 ribs; and, Over inflation: Flattened diaphragms, >than 9 ribs on chest *X* ray.

Institutional ethics committee approved the study and informed consent was taken before starting HFOV. Baseline characteristics for survivors and non-survivors were compared using student's '*t*' test, and odds ratios were calculated using Chi square test. The significance level for all tests is set at $P<0.05$.

RESULTS

Ninety seven neonates were treated with HFOV after failing CMV during the study period. Prematurity and HMD constituted the majority of babies who received HFOV (***Table* I** and **II**). Median Age of presentation was 1 day (1-23 days). 73 babies were shifted to HFO at a MAP of 12-15mmHg, four were shifted at MAP 10 -12mmHg (airleaks) and twenty at MAP of >16mmHg. The PIP values ranged from 22-36 (mean 28) and low PIP levels were seen in ELBW babies. The mean PEEP

TABLE I BASELINE VARIABLES OF OSCILLATED BABIES

Gestation (weeks)	Total Admitted Babies	Ventilated	HFOV*	Antenatal steroids†			Survival in oscillated babies (%)
				0	1	2	
Up to 26	46	41	11	1	2	8	4 (36.4)
27 – 28	82	64	6	1	3	2	2 (33.3)
29 – 30	256	90	8	0	3	5	4 (50)
31 – 32	312	85	6	2	1	3	4 (66.7)
33 – 34	388	113	10	6	2	2	6 (60)
35 – 36	385	98	8	7	1	0	7 (87.5)
37 and above	767	184	48	0	0	0	30 (62.5)
Total	2236	675 (30.2%)	97	17	12	20	57 (58.8)

** High-frequency oscillatory ventilation; †No. of times antenatal steroids used in babies on HFOV.*

TABLE II DISEASE SPECIFIC SURVIVAL

Cause of respiratory distress in babies who were oscillated (*n*)	Survival (%)	Odds Ratio for death (C I)
HMD (*n*=45)	30 (66.66)	0.54 (0.23-1.23)
PPHN (*n*= 37)	24 (64.86)	0.66 (0.28-1.54)
Pulmonary hemorrhage (*n*=15)	8 (53.33)	1.29 (0.42- 3.92)
Sepsis (*n*=20)*	9 (45)	2.02 (0.74-5.46)
MAS (*n*=22)	17 (77.27)	0.33 (0.11-1)
NEC (*n*=2)	0	–
CDH (n=12)	4 (33.33)	3.31 (1.01-11.88)
CHD (*n*=3)	1 (33.33)	2.94 (0.25-33.66)

** 7/20 babies had fungal sepsis, 2 survived; HMD: Hyaline membrane disease, PPHN: Persistant pulmonary hypertension of Newborn, MAS: Meconium aspiration syndrome; NEC: Necrotizing enterocolitis; CDHR: Congenital diaphragmatic hernia; CHD: Congenital heart disease.*

TABLE III PRIMARY OUTCOME MEASURES STUDIED

Parameter	CMV mean(SD)	2 hrs after rescue HFOV mean (SD)	*P* value
$AaDO_2$	518.42 (124.8)	477.51 (144.3)	0.048
FiO_2 %	0.905 (16)	0.881 (17.6)	0.348
pH	7.23 (0.14)	7.37 (0.14)	<0.001
$PaCO_2$	55.02 (17.7)	35.60 (8.2)	<0.0001
PaO_2	58.28 (27.2)	106.08 (72.5)	<0.001
P/f ratio	69.36 (44.2)	121.9 (86.3)	<0.001
Oxygen index	27.41 (21.2)	20.84 (17.2)	0.028
Lung recruitment (ribs)	6.67(0.6)	7.92 (0.87)	0.001

$AaDO_2$: Arterial-alveolar oxygen difference; FiO_2 ; Fractional concentration of Oxygen in inspired air;P/f ratio.

was 6.1mmHg (3-9), babies were shifted to HFO at lower PEEP in air-leaks, CDH and in idiopathic PPHN. Mean age at initiation of rescue HFOV was 2.61 days (range 1-29 days) and mean duration of ventilation was 62.02 hours (range 6-209 hours).

Of 97 neonates who were oscillated 57 (58.77%) improved and survived with comparable survivals across each gestations. OI <15 was seen in a total of 52 babies in the first two hours of oscillation, of which 41 survived, and OI <10 was seen in 32 babies, of which 24 survived. Decrease in OI, p/f ratio, $AaDO_2$ and improvement in pH, PCO_2, PO_2 with good lung recruitment was seen within 2 hours in all the babies (***Table* III**).

DISCUSSION

HFOV is a safe and effective rescue technique in the treatment of neonates with respiratory failure in whom CMV fails [6]. The results of our study show that rescue HFOV improved oxygenation, ventilation, lung recruitment and better oxygenation indices and there was no increased incidence of IVH or airleaks. The HIFO trial [7] found that in the first 24 hours after randomization, infants on HFOV required lower FiO_2 and had lower $PaCO_2$ when compared with infants on CMV. Provos study [8] found improved oxygenation after the baby was oscillated and better p/f ratios with decrease in FiO_2 requirement. Jaballah, *et al*. [6] in neonates treated for acute respiratory failure found significant decrease in MAP, FiO_2, OI, and $AaDO_2$ after starting HFOV, PaCO2 decreased significantly after one hour of HFOV. Similar results were reported by Sarnaik, *et al*. [9] in 31 children, 6 hours after institution of HFOV.

Survival rates in our study were 58.8% as compared to 75% reported previously but the population studied was much older and they had excluded four patients who died few hours after shifting from HFOV [10]. In our study, babies with CDH (OR of death 3.3), sepsis (OR 2) and babies with pulmonary hemorrhage (OR 1.29) had high mortality and affected the overall survival rates. The response to HFOV in babies who avoided ECMO in a study by Carter, *et al*. [5] was 46% and babies who failed HFOV were treated with ECMO. However, we had to continue HFOV in the babies who failed because of absence of ECMO at our center.

The absence of a control group in our study precludes firm conclusions about potential benefits of rescue HFOV. The efficacy could only be demonstrated by changes in the oxygenation, pH and ventilation, which improved significantly after HFOV. FiO_2 were still high in the HFOV group as the oxygen requirements in most of the babies who died

WHAT THIS STUDY ADDS?

- High frequency oscillatory ventilation was found to improve short term oxygenation and ventilation in neonates who failed CMV, and was not associated with increased risk of PVL or IVH.

were very high, inspite of HFOV and recruitment of the lungs. Hypocarbia should be monitored closely in babies who are on HFOV and has been associated with PVL in preterm babies [11], as two babies had PCO_2 of 18 mm Hg in the first blood gas on the oscillator (both term babies with PPHN) and six babies had PCO_2 between 20 to 30 mm Hg. There is a need for further randomized controlled trials for rescue HFOV, especially in countries where facilities for ECMO are not available.

Contributors: CDK conceived and designed the study, and would act as the guarantor; PPK was responsible for analysis of the data and drafting the paper; KS and VL was responsible for collection of data; AVL and FS participated in protocol development and helped in drafting the paper. The final manuscript was approved by all the authors.
Funding: None.
Competing interests: None stated.

REFERENCES

1. Henderson-Smart DJ, De Paoli AG, Clark RH, Bhuta T. High frequency oscillatory ventilation versus conventional ventilation for infants with severe pulmonary dysfunction born at or near term. Cochrane Database Syst Rev. 2009;3: CD002974.
2. Graciano AL, Fried EB. High-frequency oscillatory ventilation in infants and children. Semin Perin Curr Opin Anaesthesiol. 2002;15:161-6.
3. Bunnell JB. High-frequency ventilation: general concepts. *In*: Donn SM, Sinha SK, editors. Neonatal Respiratory Care. 2nd edition. Philadelphia: Mosby, Inc. 2006. p. 222-30.
4. Clark RH, Yoder BA, Sell MS. Prospective, randomized comparison of high-frequency oscillation and conventional ventilation in candidates for extracorporeal membrane oxygenation. J Pediatr. 1993;124:447-54.
5. Carter JM, Gerstmann DR, Clark RH, Snyder MG, Cornish JD, Null DM, *et al*. High-frequency oscillatory ventilation and extracorporeal membrane oxygenation for the treatment of acute neonatal respiratory failure. Pediatrics. 1990;85:159-64.
6. Ben Jaballah N, Mnif K, Khaldi, Bouziri A, Belhadj S, Hamdi A. High frequency oscillatory ventilation in term and near term infants with acute respiratory failure: early rescue use. Am J Perinatol. 2006;23:403-11.
7. HIFO Study Group. Randomized study of high-frequency oscillatory ventilation in infants with severe respiratory distress syndrome. J Pediatr. 1993;122:609-19.
8. Gerstmann DR, Minton SD, Stoddard RA, Meredith KS, Monaco F, Bertrand JM, *et al*. The Provo multicenter early high frequency oscillatory ventilation trial: Improved pulmonary and clinical outcome in respiratory distress syndrome. Pediatrics. 1996;98: 1044-57.
9. Sarnaik AP, Meert KL, Pappas MD, Simpson PM, Lieh-lah MW, Mary W, *et al*. Predicting outcome in children with severe acute respiratory failure treated with high-frequency ventilation. Crit Care Med. 1996;24:1396-1402.
10. Ben Jaballah N, Khaldi A, Mnif K, Bouziri A, Belhadj S, Hamdi A, *et al*. High-frequency oscillatory ventilation in pediatric patients with acute respiratory failure. Pediatr Crit Care Med. 2006;7:362-7.
11. Wiswell TE, Graziani LJ, Kornhauser MS, Stanley C. Effects of hypocarbia on the development of cystic periventricular leukomalacia in premature infants treated with high-frequency jet ventilation. Pediatrics. 1996; 98:918-24.