

Original Research Article

Outcome of neonates receiving high frequency oscillation ventilation in a tertiary care institution

Kalpana M. S.^{1*}, Kalyani S.²

¹Department of Pediatrics, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu, India

²Department of Neonatology, London Hospital, Kuwait, Kuwait

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*Correspondence:

Dr. Kalpana M. S.,

E-mail: kalpana10267@gmail.com

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ABSTRACT

Background: High-frequency ventilation is defined as ventilation at a frequency greater than four times normal respiratory rate. HFOV has been used as alternative to conventional ventilation and in respiratory failure of various etiologies. The aim of the study was to identify the indications of neonates receiving HFOV, following failure of conventional ventilation.

Methods: Total 93 neonates were enrolled in the study who received HFOV. The criteria for starting HFOV, the ventilator settings, CBG and ABG analysis, oxygenation index (OI), duration of ventilation and complications of ventilation were recorded during CMV and subsequently when shifted over to HFOV. Outcomes such as oxygenation, lung recruitment and ventilation and survival were monitored.

Results: Total 66 neonates (71%) were term babies. Among the 27 preterm 18 (18.4%) were 33-34±6 weeks of gestational age. Male were 50 in number (53.8%) and female were 43 (46.2%). The male: female ratio was 50:43. Disease specific survival analysis revealed more than 50% survival in cases of pneumonia, collapse, air leak, MAS and pulmonary hemorrhage. 16 out of 33 babies (48.5%) with PPHN survived. All 3 babies with CDH expired. Of the 93 neonates included in the study, 53 (57%) of them were discharged home. The major complications noted while on HFOV were- 38 neonates (40.8%) had air leaks. Instead of, ventilator associated pneumonia was present in 42 of them (45.1%) and none of them developed IVH or NTB (Necrotising tracheo bronchitis).

Conclusions: HFOV is a safe and effective technique in the treatment of neonates with respiratory failure in whom CMV fails. The results of present study show that rescue HFOV improved oxygenation, ventilation and lung recruitment and there was no increased incidence of IVH.

Keywords: HFOV, Neonates, Respiratory failure, Ventilation

INTRODUCTION

Respiratory failure is still a major cause of mortality and morbidity in new born infants. Hyaline membrane disease (HMD) is the most common condition requiring ventilation in preterm neonates. Various modes of ventilation have been tried with an aim to reduce this mortality. Conventional mechanical ventilation (CMV) has played a vital role in saving the lives of neonates with respiratory failure.¹ There have been certain clinical

conditions where the neonates have required higher settings on conventional mechanical ventilation (CMV) which might lead to barotraumas and volutrauma.

High frequency oscillatory ventilation (HFOV) has proved useful in treating respiratory failure in both preterm and term neonates. Improving arterial oxygenation, lesser barotraumas and the reduction in the incidence of air leak are the commonly reported advantages of HFOV.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 extra corporeal membrane oxygenation (ECMO), or result in death. High frequency oscillatory ventilation has served as a bridge between conventional mechanical ventilation (CMV) and extra corporeal membrane oxygenation (ECMO).³

Studies suggest that HFOV is a better rescue therapy and also decreases the requirement of ECMO.^{4,5} High frequency oscillatory ventilation is a type of mechanical ventilation that uses a constant distending pressure. Mean airway pressure (MAP) with pressure variations oscillating around the MAP at very high rate (up to 900 cycles per minute). This creates small tidal volumes, often less than the dead space.

In conventional ventilation, large pressure changes (the difference between PEEP and PIP) create physiological tidal volume and gas exchange is dependent of bulk convection (expired gas exchanged for inspired gas).

HFOV relies on alternative mechanisms of gas exchange such as molecular diffusion, Taylor dispersion, turbulence, asymmetric velocity profiles, pendelluft, Cardiogenic mixing and collateral ventilation.⁶

The large pressure changes and volumes associated with conventional ventilation have been implicated in the pathogenesis of ventilator induced lung injury (VILI) and chronic lung disease.⁷ Animal studies support that high frequency oscillatory ventilation may reduce lung injury.⁸

At present HFOV is indicated as a rescue therapy in failure of conventional ventilation in the term infant (Persistent pulmonary hypertension of the newborn (PPHN), meconium aspiration syndrome (MAS)).^{9,10}

HFOV is indicated in failure of conventional ventilation in preterm infants (serve RDS, PIE, pulmonary hypoplasia), or to reduce barotrauma when conventional ventilation settings are high. HFOV is not as yet to be of benefit in the elective or rescue treatment of preterm infants with respiratory dysfunction and may be associated with an increase in intra ventricular hemorrhage.¹¹

Role of HFOV

- As a rescue strategy when conventional ventilation is failing
- Air leak syndromes (pneumothorax, pulmonary interstitial emphysema)
- PPHN, pneumonia
- Pulmonary hypoplasia with CDH
- ECMO (before and during)

The aim of the study was to know the indications of neonates receiving high frequency oscillation ventilation, following failure of conventional ventilation in a tertiary care institution.

METHODS

The study was a prospective observational study conducted from September 2016 to April 2018 at Institute of child health and hospital for children, Chennai, Tamil Nadu a 40 bedded tertiary level NICU.

During the study period, 368 babies were ventilated, out of which 93 babies who required oscillation as per the unit protocol were included in the study.

Inclusion criteria

- All newborns receiving High Frequency Oscillatory Ventilation, following failure of conventional ventilation will be included in the study.
- All newborns receiving HFOV along with Nitric oxide were enrolled.

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, 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 babies were started on a MAP of 3 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 FiO₂.

The amplitude was adjusted based on the chest wiggle; frequency was started at 10 Hz for both preterm and 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. The baby was kept on the Sensormedix 3100 A oscillators, and rest of the treatment was given as per the standard unit protocols and guidance chart.

Criteria for starting HFOV

The criteria for starting HFOV were high pressure on CMV, inadequate oxygenation, ventilation, inadequate recruitment in spite of high PEEP, deterioration on CMV in spite of high pressures, and severe PPHN. Neonates who were referred from other hospitals after failing CMV and/or were unstable on CMV were connected to CMV at our NICU, adjustment of PIP, PEEP and FiO₂ were made and MAP was recorded. These babies were also later connected to Sensormedix 3100 A oscillator.

Outcome measures

The ventilator settings, ABG analysis (done as soon as possible after HFOV but in few instances took up to 3 hours), Oxygenation index (OI), duration of ventilation, and complications of ventilation were recorded during CMV and subsequently when shifted over to HFOV. Outcomes were oxygenation, lung recruitment, ventilation, and survival. Institutional ethics committee approved the study.

Statistical analysis

Baseline characteristics for survivors and non survivors were compared using Student’s ‘t’ test and odds ratios were calculated. The significance level for all tests is set at p >0.05.

RESULTS

Total neonatal admissions during the study period from September 2016 to April 2018 were 1623. Number of neonates who were ventilated was 368 (22.67%). The neonates who were connected to High frequency oscillatory ventilation were 93 (25.27%).

Age distribution (in weeks)

Term >37 weeks / preterm <37 weeks.

Among the 93 neonates included in the study 27(29%) were preterm and 66(71%) were term babies

Age distribution of the preterm babies

Among the 93 neonates included in the study, 5(5.4%) were 31-32±6 weeks, 18 (19.5%) were 33-34±6 weeks and 4 (4.2%) were 35-36±6 weeks.

Sex distribution

Among the neonates in the study 50 (53.8%) were males and 43 (46.2%) were females.

Birth weight

Birth weight distribution of the neonates included in the study.

Among the 93 neonates included in the study, 12 neonates (12.9%) weighed 1000-2000 gm, 45 (48.4%) weighed 2010-3000 gm and 36 (38.7%) weighed 3010-4000 gm (Figure 1).

Cardio vascular system examination - presence of shock

Of the 93 neonates included in the study, 71 (76.3%) had features of shock and 22 (23.7%) did not have features of shock.

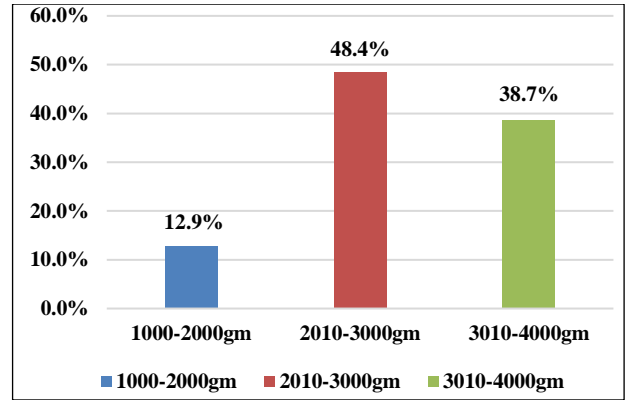


Figure 1: Birth weight distribution of the neonates included in the study.

Central nervous system examination - presence of intra ventricular hemorrhage (IVH) before connecting to HFOV

Among the 93 neonates included in the study 14 (15.1%) had IVH before connecting to HFOV, 79 (84.9%) did not have IVH before connecting to HFOV.

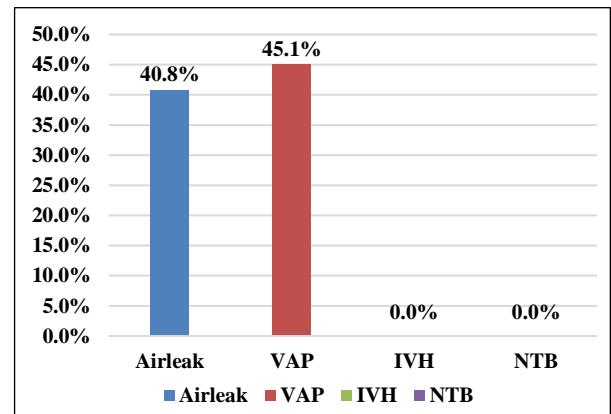


Figure 2: Complications.

Cause of respiratory distress in babies who were oscillated

Table 1: Cause of respiratory distress in babies who were oscillated.

Cause of respiratory distress in babies who were oscillated	No.	% age
Pulmonary hemorrhage	6	6.45
MAS	20	21.28
Air Leak	20	21.28
CDH	3	3.22
Pneumonia	12	12.90
PPHN	33	35.48
Collapse	7	7.52

Among the 93 neonates included in the study, PPHN was the commonest cause of respiratory distress for which the

babies were oscillated. PPHN was present in 33 (35.48%). This was followed by MAS in 20 (21.2%) and air leak in 20 (21.2%). Of the rest 6 (6.45%) had pulmonary hemorrhage, congenital diaphragmatic hernia in 3 (3.22%), pneumonia was present in 12 (12.9%) and collapse was present in 7 (7.52%). Many neonates had combination of features, but the primary cause of respiratory distress was taken into account (Table 1).

Primary outcome measures

The primary outcome measures were studied with respect to FiO₂, Oxygen saturation (SaO₂), pH, oxygenation index (OI) and expansion on chest X ray (CXR) and these measures were compared with Conventional mechanical

ventilation (CMV) and high frequency oscillatory ventilation (HFOV) and significant p-value was analyzed.

The primary outcomes studied were as above, the p value was significant (<0.05) in the parameters like FiO₂, SaO₂, pH, oxygenation index (OI) and CXR expansion, whereas the p-value was not significant (p=0.345) in the pCO₂ (Table 2).

Settings on HFOV: MAX MAP (mm Hg)

Among the 93 neonates included in the study 65 (69.9%) needed MAP of 16-20, 20 (21.5%) needed MAP of 21-25, and 8 of the (8.6%) needed a MAP of 26 -30.

Table 2: Primary outcome measures.

Parameter	CMV mean (SD)	3 hours after rescue HFOV mean (SD)	P-value
FiO ₂	94.41 (4.2)	88.06 (4.7)	<0.05 (S)
SaO ₂	79.97 (6.06)	85.13 (5.9)	<0.05 (S)
pH	7.30 (0.045)	7.33 (0.054)	<0.05 (S)
pCO ₂	49.32 (11.61)	47.96 (8.9)	0.345 (NS)
Oxygenation index (OI)	20.29 (1.61)	21.21 (2.7)	<0.05 (S)
CXR expansion	7.27 (1.023)	8.51 (1.028)	<0.05 (S)

S-significant / NS-not significant, P value <0.05 is considered significant.

Settings on HFOV-Max P (amplitude)

Among the 93 neonates included in the study 31 (33.3%) received an amplitude of 26-30, 45 (48.4%) received an amplitude of 31-35 and 17 (18.3%) received an amplitude of 36- 40.

Table 3: Number of ventilated days on HFOV.

No. of ventilated days on HFOV	No.	%age
1	1	1.1
1	1	1.1
3	1	10.8
4	26	40.9
5	17	18.3
6	13	14
8	5	5.4
9	8	8.6
10	2	2.2
11	2	2.2
12	1	1.1
14	1	1.1

Settings of HFOV-max frequency

Among the 93 neonates included in the study 8 (7.5%) received a frequency of 7, 39 (41.9%) received a

frequency of 8, 27 (29%) received a frequency of 9, 19 (21.6%) received a frequency of 10.

Number of ventilated days on HFOV

Among the 93 neonates included in the study 1 (1.1%) was ventilated for 1 day, 1 (1.1%) for 2 days, 10 (10.8%) for 3 days, 26 neonates (40.9%) for 4 days, 17 (18.3%) for 5 days, 13 (14%) for 6 days, 5 (5.4%) for 8 days. 8 (8.6%) for 9 days, 2 (2.2%) for 10 days, 2 (2.2%) for 11 days, 1 (1.1%) for 12 days and 1 (1.1%) for 14 days (Table 3).

Number of ventilated days on HFOV + iNo

Among the 93 neonates included in the study 81(87.1%) did not receive iNo with HFOV and 12 (12.9%) received iNo along with HFOV

Table 4: No of ventilated days on HFOV + iNo.

HFOV + iNo	No. of ventilated days	No.	%age
2		3	25
3		3	25
4		4	33.3
5		2	16.6

Among the 12 neonates who received HFOV along with iNo, 3 (25%) received HFOV and iNo for 2 days, 3

(25%) received HFOV and iNo for 3 days, 4 (33.3%) received HFOV and iNo for 4 days and 2 (16.6%) received HFOV and iNo for 5 days (Table 4).

Complications

Among the 93 neonates included in the study 38(40.8%) had air leak while on HFOV, 42 (45.1%) had ventilator associated pneumonia. None of them developed IVH or necrotizing tracheo bronchitis (Figure 2).

Outcome

Among the 93 neonates included in the study 53 (57%) were discharged home and 40 (43%) expired.

Baseline variables of oscillated babies

Among the 93 neonates in present study, 66 were term babies and 37(56%) of them survived. In the gestational

age group of 31-32weeks±6 days, 5 babies received HFOV and 3(60%), survived. Among those who were 33-34weeks±6days, 18 were on HFOV and 12 (67%) babies survived. In the gestational age group of 35-36weeks±6days, 4 babies were on HFOV and only 1 neonate (25%) survived (Table 5).

Disease specific survival

Out of the 93 neonates enrolled in the study, PPHN was present in 33 of them, and 16 (48.5%) babies, survived, 6 neonates had pulmonary hemorrhage and 5 (83%) survived, MAS was present in 20 babies and 11(55%) babies survived. Out of the 3 neonates with congenital diaphragmatic hernia (CDH), none of them survived including the one who was on ECMO. Air leak was present in 20 neonates and 16 (80%), of them survived. Out of the 12 neonates with pneumonia, 6 (50%) neonates survived. 7 babies had collapse lung, out of which 4 (57%) survived. Out of the 21 preterm babies with HMD, 11 (52.4%) survived (Table 6).

Table 5: Baseline variables of oscillated babies.

Gestation (weeks)	No. of babies ventilated	No. of babies on rescue HFOV	Survival in oscillated babies (%)
31-32±6 weeks	26	5	3 (60)
33-34±6 weeks	45	18	12 (67)
35-36±6 weeks	82	4	1 (25)
≥37 weeks	215	66	37 (56)

Table 6: Disease specific survival.

Cause of res distress in babies who were oscillated (n)	Survival %	Odds ratio for death (CI)
PPHN (n=33)	16 (48.5)	1.27 (0.849 - 1.906)
Pulmonary hemorrhage (n=6)	5 (83)	0.662 (0.442 - 0.993)
MAS (n=20)	11(55)	1.05 (0.672 - 1.63)
CDH (n=3)	0	-
Air leak (n=20)	16 (80)	0.634 (0.46 - 0.86)
Pneumonia (n=12)	6 (50)	1.16 (0.64 - 2.1)
Collapse (n=7)	4 (57)	0.997 (0.51 - 1.94)
HMD (n=21)	11 (52.4)	1.114 (0.709 - 1.75)

DISCUSSION

HFOV, a technique of rapid ventilation with use of very small tidal volume has potential of reducing ventilator associated lung injuries.

HFOV as a modality of neonatal ventilation has been infrequently reported from India. Poddutoor PK et al, conducted a study at rainbow children’s hospital to study the efficacy of rescue HFOV in improving the oxygenation and respiration in neonates with acute respiratory failure after failing conventional mechanical ventilation.¹² A prospective descriptive study was done at institute of child health to know the indications for which

neonates were connected to HFOV; the parameters on CMV and HFOV were noted and were followed till outcome-death/discharge.

In the study by Poddutoor PK et al, 675 babies were ventilated from January 2006-June 2009 (3.5 years), 675 babies were ventilated out of which 97 babies received HFOV.¹² In present study period of 20 months from September 2016-April 2018, 1623 neonates were ventilated out of which 93 babies received HFOV.

In comparison to the study by Poddutoor PK et al, where prematurity and HMD constituted the majority of babies receiving HFOV, in present study, MAS-20 babies,

PPHN-33 babies and airleak-20 constituted the majority of babies connected to HFOV.¹²

Among the 27 preterm babies 21 of them (77.7%) had hyaline membrane disease (HMD) and received surfactant.

Total 41 babies were shifted at a MAP of 16-20 mm Hg. 12 babies at MAP of 21-25 mm Hg and 8 babies at MAP of 26-30 mm Hg.

In present study, none of the babies were shifted to HFOV at MAP of 10-12 mm Hg whereas in Poddutoor PK et al, study, 4 babies who had air leak were shifted to HFOV at a MAP of 10-12 mm Hg.¹²

The PIP values in present study ranged from 20-32 (mean-28) and the low PIP values were seen in low birth weight babies. The mean was in par with the study by Poddutoor PK et al, conducted at Hyderabad.¹²

In present study, the mean PEEP was 5 mm Hg (3-8 mm Hg), the babies were shifted to HFOV at lower PEEP in air leaks and PPHN. In comparison, mean PEEP of 6.1 mm Hg was used in the study Poddutoor PK et al.¹²

In present study, the Mean age at initiation of rescue HFOV was 4 days (range,1-24 days) as compared to the study of Poddutoor PK et al, where the mean age at initiation of rescue HFOV was 2.61 days (range:1-29 days).¹²

In present study, out of the 66 term babies, 33 of them had PPHN and 16 (48.55) survived. In present study of 93 neonates, none of them developed IVH/PVL when they were connected to HFOV.

Out of the 93 neonates who received HFOV, 2 babies with NEC received HFOV and had better oxygenation and ventilation. This is reassuring and is reinforced by case series of 8 preterm infants with increased intra-abdominal pressure mostly due to NEC, as reported by Fok TF et al.¹³

Of the 93 neonates who received HFOV, 27 were preterm and 3 of them developed PIE.

Wong W et al, quoted that tracheal damage and Necrotising tracheo bronchitis (NTB) as a complication of HFOV.¹⁴ In present study, although a direct laryngeal examination was not done (in detail), none of the babies had devastating NTB as a complication of HFOV.

In the study by Poddutoor PK et al, twelve of them had CDH and none of them was on ECMO as the facility was not available.¹² Out of the 93 ventilated babies who received HFOV in present study, 3 had CDH, none of them survived. One neonate was on extra corporeal membrane oxygenation (ECMO) for 11 days.

The oxygenation index (OI) was mildly increased in the babies who were on HFOV as compared to CMV whereas in the study by Poddutoor PK et al, there was an overall decrease in OI.¹²

Of the 93 oscillated babies in present study 53 (57%) improved and survived which is in nearly at par with the Poddutoor PK et al, study where 57 (58.77%) out of 978 babies survived.¹²

In present study 12 neonates received inhaled Nitric oxide (iNO) along with HFOV and improved. Comparing the disease specific survival as regards to the study by Poddutoor PK et al, 45 babies with HMD were oscillated and 30 (66.66%) survived, whereas in present study, out of the 21 babies who had HMD and 11 of them (52.4%) survived and the survival percent in present study is lesser than his study.¹² Among the babies with PPHN, in the study by Poddutoor PK et al, 37 neonates had PPHN, 24 of them (64.86%) survived, whereas in present study, out of the 33 neonates with PPHN, 16 (48.5%) survived which is also lesser than his study.¹² In present study 6 babies had pulmonary hemorrhage, 5 (83%) of them survived whereas in the Hyderabad study by Poddutoor PK et al, among the 15 babies with pulmonary hemorrhage, only 8 (53.33%) had survived; our survival percentage has been higher in babies with pulmonary hemorrhage.¹²

Among the 20 babies with MAS in present study, 11 of them (55%) have survived, in comparison with the similar prospective study by Poddutoor PK et al, where, out of the 22 babies with MAS, 17 neonates (77.27%) had survived.¹² Our survival percentage has been lesser in babies with MAS. In the 2 babies with NEC, none of them survived in the study by Poddutoor PK et al, whereas, in present study, 2 neonates had NEC and both of them survived.¹²

In contrast to the above results, all the 3 babies with congenial diaphragmatic hernia (CDH) expired, including the one who was on ECMO, whereas in the similar study by Poddutoor PK et al, out of the 12 babies with CDH, one third of them-4 (33.33%) survived.¹² Comparing the primary outcome measures, between present study and the prospective study from Hyderabad, among the term babies who were 48 out of the total 97 babies in the Hyderabad study, survival was 30 (62.5%), where as in present study, there were 66 term babies and 37 of them survived (56%).

CONCLUSION

HFOV is a safe and effective technique in the treatment of neonates with respiratory failure in whom CMV fails. The results of present study show that rescue HFOV improved oxygenation, ventilation and lung recruitment and there was no increased incidence of IVH. There was a marginal increase in the incidence of air leak probably due to delayed reduction in the MAP or settings on

HFOV that led to barotraumas. There is a need for further randomized controlled trials for rescue HFOV, especially in countries where facilities for ECMO are available, but expensive.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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