High Frequency Ventilation in Neonates

W Wong, TF Fok, PC Ng, KL Cheung

Abstract

There are many examples of high frequency ventilation (HFV) in nature. The key difference from conventional mechanical ventilation (CMV) is the usage of unusually high rates and low tidal volumes. The cyclic changes in lung volume during large tidal ventilation are believed to be an important factor in causing lung injury. Many randomized controlled trials have been conducted to test the efficacy of HFV in the reduction of chronic lung diseases in premature infants. Outcomes of the early trials, including the HIPI study, were disappointing. Subsequent studies, in which a strategy to promote lung recruitment and maintenance of lung volume was used, showed favourable outcomes. HFV used with a high lung volume strategy, applied by experienced neonatologists under vigorously controlled conditions, do offer some protection from lung injury in preterm infants. However it is not without complications. Meta-analysis of randomized controlled trials suggested that the benefits of HFV in reducing chronic lung diseases appeared to be outweighed by concerns about the increased rates of pulmonary air leak and severe intraventricular haemorrhage. Experience is an important element in the safe and efficient use of HFV particularly in premature infants. Many uncertainties about the use of HFV, such as the long term risk-benefit ratio, still remain and await further research.

Key words

Chronic lung diseases; High frequency ventilation; Mechanical ventilation; Neonates

Introduction

A very important cause of mortality and morbidity of very-low-birth-weight infants (VLBW) is lung injury due to mechanical ventilation. Physiologically we breathe by generating a negative pressure within the lung but unfortunately almost all currently used mechanical ventilators generate positive pressure. Animal studies using premature animals with respiratory distress syndrome (RDS) have shown that both high pressure (barotrauma) and large tidal volume (volutrauma) damage the pulmonary capillary endothelium, alveolar and airway epithelium, and basement membrane. This mechanical damage further leads to a cascade of injuries resulting in leakage of fluid, protein and blood into the airways, alveoli and interstitial spaces, resulting in inhibition of surfactant activity and further lung injury. The cyclic changes in lung volume during large tidal ventilation are believed to be more important than airway pressure changes, hence a ventilator strategy that avoids large tidal volume may reduce lung injury. For this reason, considerable effort has been given in the past 10-15 years to the application of high frequency ventilation (HFV) in neonates with respiratory failure. This ventilatory technology allows ventilation with unusually high rates and low tidal volumes.

Many clinical studies have been carried out to test the efficacy and safety of HFV. Controversies and uncertainties still exist in many aspects, such as the indications for use in neonates, the effectiveness in preterm infants and the
benefit in reducing bronchopulmonary dysplasia (BPD) when compared with CMV. This review article aims to provide an overview on the application of HFV in neonates with particular emphasis on the results of clinical studies.

**Definition of HFV and Mechanisms of Gas Exchange**

There is no unified definition of HFV, but most authors would accept the following two inclusions: (1) high ventilation rate of at least 2 Hz and (2) ventilation at small tidal volumes that are smaller than anatomic dead space. The key difference from CMV is the usage of unusually high rates and low tidal volumes. Because the tidal volume is ever smaller than the dead space, the gas transport during HFV cannot be explained by bulk flow theory as in CMV.

There are many examples of HFV in nature (Table 1). However the exact mechanism of gas exchange is not fully understood, it is likely that several mechanisms are playing a role at the same time. Proposed mechanisms that can enhance gas exchange during HFV are listed in Table 2.2 As in CMV, molecular diffusion is the most important mechanism at the alveolar-capillary membrane.

**Types of High-frequency Ventilators**

Three types of HFV ventilators are approved for use in infants in the United States: high frequency oscillatory ventilator (HFOV), high frequency flow interrupter (HFFI) and high frequency jet ventilator (HFJV). HFJV is not widely used in neonates and is not available in Hong Kong.

HFOV employs either a piston or diaphragm to oscillate a bias flow of gas to generate both positive and negative pressure fluctuations termed as amplitude. There are not a lot of adjustable parameters in the machine. These include mean airway pressure (MAP), frequency and amplitude. Frequency is usually fixed for a particular patient group. The recommended range is 10-15 Hz for premature infants and 8-10 Hz for term infants. It is the authors' departmental policy to use 12 Hz for premature infants and 8 Hz for term infants. Inspiratory time is set at 33% of the oscillatory cycle.

HFFI has both CMV and HFV functions. To produce HFV the flow of gas is interrupted by a valve which acts like a shutter working at a high rate. In addition to those used in CMV, the operator adjustable parameters also include frequency and amplitude. Oxygenation is dependent on positive end expiratory pressure (PEEP), acting as MAP. Carbon dioxide removal is affected by the amplitude and, if sigh breathes are used, the difference between peak inspiratory pressure (PIP) and PEEP.

**Physiological Effects of HFV**

### Ventilation

Ventilation in CMV is calculated by the product of respiratory rate \( f \) times tidal volume \( V_T \). In contrast ventilation in HFV is calculated by the equation \( f^a \times V_T^b \) where "a" is found to be between 0.75 and 1.24; and "b" is between 1.5 and 2.2.3 For clinical application the equation is simplified to \( f \times V_T^2 \). Thus \( CO_2 \) elimination is more strongly affected by changes in \( V_T \) than in frequency. This explains why even small changes in \( V_T \) would produce big effect on ventilation. Furthermore due to the characteristics of the HFV machine, the delivered tidal volume is inversely related to frequency. To avoid wide variations in the delivered tidal volume the oscillatory rate is generally held constant during the clinical application of HFV. However

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**Table 1  Examples of HFV in nature**

- Panting dogs
- Humming birds
- Patients with severe pulmonary emphysema
- Mixing of pulmonary gases due to dynamics of cardiac contraction cycles

**Table 2  Proposed mechanisms that can enhance gas exchange during HFV²**

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<tr>
<td>(1)</td>
<td>Direct ventilation of most proximal alveoli units by bulk convection</td>
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<td>(2)</td>
<td>Pendalluft effect – asynchronous flow among alveoli due to asymmetries in airflow impedance. This cause gas to recirculate among lung units and improve gas exchange</td>
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<td>(3)</td>
<td>Turbulence in the large airways causing enhanced gas mixing</td>
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<td>(4)</td>
<td>Turbulent flow with lateral convective mixing</td>
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<td>(5)</td>
<td>Taylor dispersion – laminar flow with lateral transport by diffusion</td>
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<td>(6)</td>
<td>Collateral ventilation through non-airway connections between neighbouring alveoli</td>
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<td>(7)</td>
<td>Asymmetric velocity profiles – convective gas transport is enhanced by asymmetry between inspiratory and expiratory velocity profiles that occur at branch points in the airways.</td>
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any decrease in the diameter of the endotracheal (ET) tube can reduce delivered tidal volume significantly and hence produces a large adverse effect on carbon dioxide removal during HFV. Secretions in the airways would produce similar effect as decrease in diameter of ET tube. For this reason tracheal care is an important element of patient care during HFV.

**Oxygenation**

Both CMV and HFV are similar in the strategies for oxygenation. Oxygenation is determined by lung volume (affected by MAP) and FiO₂. In both types of ventilation it is important to maintain adequate lung volume to prevent atelectasis and to preserve surfactant function to achieve adequate oxygenation. During HFV adequate MAP should be used to recruit alveoli and maintain lung volume above functional residual capacity (FRC). In contrast to CMV, lung volume is maintained at a relatively constant level during HFV. The ventilation/perfusion matching would improve as a result of alveolar recruitment when lung volume increases. The near constant lung volumes in HFV results in better gas distribution and avoids the development of regional atelectasis in less compliant lung units, hence resulting in better ventilation/perfusion matching.

**Volume Delivery During HFOV**

Dimitriou et al. studied two commonly used HFOV machines, SensorMedics 3100A and SLE 2000, to determine the volume delivery during HFOV. The delivered volume was measured by a pneumotachograph system. They found that the median delivered volume was 2.4 ml/kg which was greater than the expected dead space of 2.2 ml/kg. Hence they postulated that there was actually direct alveolar ventilation during HFOV, which was estimated to be about 50% of that delivered by CMV. This helps to explain why lung damage still occurs with HFOV.

**Clinical Applications in Neonates**

The clinical indications for the use of HFV are listed in Table 3. There are no universally accepted criteria to define ventilatory failure during CMV, to indicate the use of HFV. Some criteria used are: PaCO₂ > 50 mmHg or FiO₂ requirement greater than 0.5 to maintain PaO₂ of 50 mmHg. Infants receiving HFV should be monitored continuously for their oxygenation and ventilation. They may require extra intravenous fluid to compensate the relative volume depletion resulting from redistribution of blood flow. Very often induced paralysis may be discontinued since the infants do not normally "fight" against HFV and spontaneous breathing can assist in overall ventilation and improve respiratory endurance. Similar to CMV, a higher CO₂ should be tolerated in infants with pulmonary interstitial emphysema (PIE). The attending neonatologist should not hesitate to return to CMV if HFV is not working after some time.

**Adjustments of Ventilatory Settings During HFV**

PaO₂ is affected mainly by adjustments in FiO₂ and MAP. It is usually not necessary to have a background intermittent mandatory ventilation (IMV) but if IMV is used, PaO₂ is also increased by increase in IMV rate, IMV inspiratory time and PIP.

PaCO₂ is reduced mainly by increase in HFV amplitude. However, changing the HFV frequency may have unpredictable effects on PaCO₂. As explained above, increasing the HFV frequency would lead to a decrease in delivered tidal volume, and may result in an increase in PaCO₂. Neonatologists must also be aware that excessive inflation of the lungs is an important cause of ventilatory failure, and reduction of MAP may result in significant improvement of carbon dioxide removal when lung hyperinflation is the cause of CO₂ retention. Frequent assessment of chest inflation both by clinical signs and chest radiographs (CXR) are important during the clinical application of HFV. Excessive MAP is suggested by a barrel-like chest and CXR findings of over-distended lung field such as the flattening of the diaphragm and cardiac compression. In addition to CO₂ retention, adverse effects of air-trapping also include decrease in cardiac output and impaired oxygenation. It is of utmost importance that excessive lung aeration is excluded before MAP or amplitude is further increased.

**Table 3** Indications for HFV in Neonates

<table>
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<th>Neonatal air leaks</th>
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<td>- PIE</td>
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<td>- Pneumothoraces</td>
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<td>- Pneumomediastinum</td>
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<td>- Bronchopleural fistula</td>
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As primary treatment for RDS

As rescue therapy when CMV fails

- PPHN
- Pneumonia etc.

Severe neonatal lobar emphysema

Increase in intra-abdominal pressure e.g. NEC
Randomized Controlled Trials on the Early Use of HFV in Treatment of RDS

The HIFI Study was the earliest and one of the largest multi-centre randomized controlled trials (RCT) conducted so far. The investigators compared the efficacy and safety of HFOV (n=327) with CMV (n=346) in the treatment of respiratory failure in 673 preterm infants weighing 750 to 2000 g, and showed that HFV had no benefit with regard to reduction in mortality, level of ventilatory support during the first 28 days, or BPD. Furthermore HFV was associated with a higher incidence of pneumoperitoneum of pulmonary origin, grade III & IV intraventricular haemorrhage (IVH) and periventricular leukomalacia (PVL).

A number of factors might have contributed to the disappointing results of the HIFI Study. The study was carried out in many centres without a well defined or uniform treatment protocol. There were great variations in the treatment strategies and in the types of ventilators used in the different centres. Furthermore, since HFV was still in its early stage of development when the study was conducted, many neonatologists were not familiar with its use. It was possible that the unsatisfactory outcome of some of the study infants had been the result of faulty application of the ventilation technique.

Subsequent to the HIFI Study, a number of RCTs comparing HFV with CMV in the treatment of RDS in premature infants had been conducted, showing variable results. Some of these studies adopted the "high-volume" strategy of using a higher MAP to maintain a higher lung volume, which has been shown in animal studies to result in better lung recruitment and oxygenation. In the Provo Multi-centre Early HFOV Trial, which is renowned for its meticulous study protocol, 125 neonates of 35 weeks or less in gestation were randomized to receive either HFOV (SensorMedics 3100A) or CMV (Sechrist IV-100B) starting at 2 hours of age. HFOV was commenced with a MAP 1-2 cm water greater than the mean airway pressure delivered by CMV used before switching over to HFOV. The MAP was further increased until there were clinical and radiological evidences of adequate lung recruitment (further increase in MAP not being followed by corresponding improvement in $\text{FiO}_2$, CXR showing more radiolucent lung fields and diaphragm at the level of 8th-9th posterior ribs). Compared to the CMV group, infants treated with HFOV had significantly more favourable outcomes, with less treatment failure (1.6% vs 14.8%); better survival without chronic lung disease (CLD) at 30 days (76.4% vs 55.7%); shorter duration of oxygen use in those $>1$ kg (13.2 vs 27.6 days); less number on ventilator beyond 28 days in those $\leq 1$ kg (45.9% vs 100%); less $\text{O}_2$ use at discharge (33.3% vs 49.2%); lower discharge median partial pressure of inspired oxygen (for altitude considerations) in those $\leq 1$ kg (136 vs 157 torr); less vasopressor use index beyond 120 hr (16.6% vs 42.3%); less incidence of NEC (6.2% vs 19.7%); less abnormal BAER (1.9% vs 16.0%); lower hospital cost in those $\leq 1$ kg (103.2 vs 192.5 x $10^3$) and in those $>1$ kg (32.2 vs 45.6 x $10^3$). There were no differences between the two groups in the length of hospital stay, the survival rate to discharge, or the incidence of patent ductus arteriosus, air leak, retinopathy of prematurity, and intraventricular haemorrhage.

In 1996, Bhuta et al performed a meta-analysis of the RCTs on the treatment of RDS with HFV, and concluded that while HFV had no effect on mortality (ERR: 1.05; 95% CI: 0.53-2.08), a significant beneficial effect on CLD was demonstrated by those studies which used a high volume strategy (ERR: 0.55; 95% CI: 0.33-0.90).

The conclusion of this meta-analysis was however not widely accepted. Further RCTs had been performed to compare HFV with CMV as the primary ventilation mode in preterm infants with RDS. In a study on 96 infants (gestational age <32 weeks), Rettwitz-Volk et al reported that HFOV was as safe and efficacious as CMV when used for the primary ventilation of premature infants with RDS who have been treated with surfactant. In a RCT consisting of 284 infants below 30 weeks of gestation, Thome et al however did not demonstrate any difference in the association of lung injury with HFV using a high lung volume strategy and CMV using high rate and low PIP.

Because of these conflicting findings, HFV has hitherto not been universally accepted as the primary mode of ventilation for infants with RDS. There was also doubt about the generalisability of the studies that favoured HFV. Most of these studies have been performed by investigators experienced in HFV, and the results may not be reproduced in less experienced centres. In some studies the differences in outcome may be explained by the non-standardized approach adopted for CMV, rather than due to the true benefits of HFV. When both modes of ventilation are ‘optimized,’ the differences in outcomes may no longer exist. All these considerations notwithstanding, the available data do support that HFV, when used by experienced neonatologists, is at least comparable to CMV in efficacy and safety in ventilating preterm neonates with uncomplicated RDS. To gain better understanding of the long term safety of HFV, follow-up studies on the long-term survival, lung function, and neurodevelopment of the treated infants are required.
Wong et al. 117

Rescue Therapy with HFV

Term Infants
There are only limited data on the use of HFV in term infants as a rescue therapy for severe respiratory failure or persistent pulmonary hypertension (PPHN). In a randomized crossover study reported by Clark et al., 79 infants of at least 34 gestational weeks referred for extra-corporal membrane oxygenation (ECMO) were randomized either to HFOV or CMV. Those who failed the initial treatment were switched to the alternative ventilator modality. The proportion of infants who failed their initial treatment assignment was comparable between the two groups. However of those who failed CMV, 63% responded to HFOV, which was significantly higher than the 23% who responded to CMV after failing HFOV. No significant differences were observed with regard to mortality or morbidity such as CLD, air leak and intracranial hemorrhage. This supported the use of HFV as rescue therapy in term infants with severe respiratory failure.

Use of HFV with Nitric Oxide in PPHN
An early randomized controlled trial of inhalational nitric oxide (iNO) was conducted by Kinsella et al in newborn infants with severe PPHN. 200 neonates were stratified by the predominant disease category into 4 groups: RDS (n=70), meconium aspiration syndrome (MAS) (n=58), idiopathic PPHN or pulmonary hypoplasia (n=43) and congenital diaphragmatic hernia (n=34). Infants in each group were randomly assigned to receive treatment with either iNO & CMV or HFOV without iNO. Treatment failure (PaO₂ <60 mm Hg) resulted in crossover to the other treatment. Further treatment failure after crossover would lead to combination treatment with HFOV and iNO. 74% of the patients failed initial treatment leading to crossover to the other treatment group. The success rates of crossover treatment were iNO 21%, HFOV 14%. There were however 125 patients who failed both treatment strategies. Subsequent treatment with HFOV and iNO together resulted in a 32% response rate. Of these successful cases, patients with RDS and MAS had the best response rates for HFOV+iNO. Based on these findings, Kinsella et al concluded that HFOV together with iNO was superior to CMV plus iNO or HFOV alone in treating severe PPHN.

HFOV in Infants with Increased Intra-abdominal Pressure
Severe abdominal distension leading to splinting of diaphragm is an important cause of respiratory failure in newborns. A case series of 8 preterm infants with increased intra-abdominal pressure, mostly due to necrotizing enterocolitis (NEC), was reported by Fok et al. HFOV with SensorMedics 3100A was found to be an effective rescue treatment when CMV failed to provide satisfactory ventilation and oxygenation in these patients.

Preterm Infants
The single largest randomized trial (n=176) was carried out by the HiFO Study Group to examine whether the use of HFOV would decrease air leak syndrome in infants with RDS, when compared with CMV. A high lung volume HFV strategy was used. During the first 24 hours after randomization, infants on HFOV required lower FiO₂ and had lower PaCO₂ when compared with infants on CMV. Fewer infants randomized to HFOV group subsequently had new development of air leak. No differences were observed between the two groups in the progression of air leak in those who already had leaks. However, the incidence of severe intraventricular hemorrhage (IVH) was significantly higher in infants treated with HFV, which was of great concern.

Recent Randomized Control Trials Comparing HFOV with CMV
Cochrane Database of Systematic Reviews by Henderson-Smart et al concluded that when elective HFOV with optimization of lung volume was used, there were significant reductions in the rate of CLD in survivors at 28 to 30 days (relative risk 0.53; 95% CI 0.36 to 0.76), of death or CLD at 28-30 days (relative risk 0.56; 95% CI 0.40 to 0.77), and of oxygen use at 36 to 37 weeks of postmenstrual age or discharge (relative risk 0.72; 95% CI 0.56 to 0.93). There was a significant increase in severe (grades 3 & 4) IVH and in any pulmonary air leak syndrome (relative risk 1.19; 95% CI 1.03 to 1.38). The authors concluded that the benefits of HFOV in terms of CLD appeared to be outweighed by concerns about increased rates of pulmonary air leak and severe IVH, hence HFOV could not be recommended as the routine ventilatory method for premature infants with RDS.

In a multi-centre study published recently, Johnson et al randomly assigned preterm infants of 23-28 weeks to receive either CMV or HFOV within one hour after birth. About 400 infants in each group were recruited. HFOV was delivered by one of three models (Drager Babyllog 8000, SensorMedics 3100A, or SLE 2000HFO). Initial settings were MAP of 6 to 8 cm water and a frequency of 10Hz.
Analysis of outcomes reviewed that there were no differences between the two groups in the composite primary outcome of death or CLD, the rate of treatment failure and in the secondary outcome measures including serious brain injury and air leak. They concluded that HFOV did not differ significantly from CMV in the early treatment of preterm infants with respiratory disease and that HFOV was not associated with significant increase in the incidence of major cerebral lesions, nor in the incidence of CLD.

Another randomized multi-centre (26 tertiary centres) clinical trial was conducted by Courtney et al. to determine whether infants treated with early HFOV had better survival without requiring supplemental oxygen at 36 weeks of postmenstrual age than infants treated with synchronized intermittent mandatory ventilation (SIMV). Five hundred infants weighting 601 to 1200 g requiring MAP of at least 6 cm water and FiO₂ of 0.25 or above were enrolled. Ventilation strategies that emphasized lung recruitment and avoidance of atelectasis and over-distention were used in both groups. The lung inflation was targeted at 8 to 9.5 ribs expansion but 7 to 8 ribs for infants with air leak or CLD. The initial MAP setting of HFOV was 2 cm water higher than that used for CMV. I:E ratio was set at 0.33 and frequency of 10-15 Hz was used. Ventilation was managed according to strict treatment protocols designed to optimize lung inflation and blood gas values. Moderate permissive hypercapnia with PaCO₂ 40-55 mm Hg was allowed. However in patients with CLD, air-leak syndrome or persistent hyperinflation, PaCO₂ up to 65 mm Hg was allowed. They found that HFOV infants were extubated significantly earlier than infants assigned to SIMV. More HFOV infants were alive without requiring supplemental oxygen at 36 weeks of postmenstrual age (56 % in HFOV vs 47% in SIMV). Hence for every 11 infants treated with HFOV, 1 death or CLD was prevented (absolute reduction in risk 9.2%). There was no difference in the risk of intracranial haemorrhage, cystic PVL or other complications. The authors concluded that there was a small but significant benefit of HFOV in terms of the pulmonary outcome without an increase in other complications of premature birth. HFOV offers a small but significant benefit at experienced centres and, in such settings, should be considered the first line ventilatory support in this group of very preterm infants.

Neonatologists would wonder why Johnson's UK Oscillation Study had different results from Courtney's US Neonatal Ventilation Study. Some possible explanations are postulated as follows: Courtney’s infants might be sicker, different types of ventilators were used, and there were differences in the management of ventilation. Courtney used one type of HFOV (SensorMedics 3100A) whereas Johnson used three different types. Johnson found the highest rate of death or BPD in the small number of patients treated with SensorMedics 3100A which Courtney used successfully, reflecting the differences in experience or management style among the neonatologists. The trial by Courtney et al. was conducted under rigorously controlled conditions with well-defined management protocols, while Johnson’s treatment strategies might better represent actual practice in many newborn intensive care units.

**Can HFOV Prevent BPD?**

Stark attempted to give an answer to this question by analyzing the recent literature. As shown by Courtney et al, early use of HFOV by experienced clinicians under rigorously controlled conditions offered some protection from lung injury in preterm infants at high risk. However the evidence obtained so far suggested that the choice of the mode of ventilation did not affect the pulmonary outcome, which might be influenced more by prenatal risk factors, initial resuscitation, and other aspects of neonatal care.

In inexperienced hands, HFOV may cause adverse effects including inadvertent over-distention of the lungs, impaired cardiac output and increased central venous pressure that might lead to intracranial haemorrhage. On the other hand, HFOV when applied according to strict protocols may be advantageous in the experienced centres. For most preterm infants with uncomplicated RDS, CMV with low tidal volumes and reasonable ventilation goals remain the appropriate choice.

**Hazards of HFV**

Some of the hazards of HFV are listed in Table 4. The commonest problem encountered during the clinical

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<td>- Air-trapping causing lung over-inflation</td>
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<tr>
<td>- Pulmonary interstitial emphysema</td>
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<tr>
<td>- Intraventricular haemorrhage &amp; periventricular leukomalacia</td>
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<td>- Tracheal damage</td>
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application of HFV is gas trapping leading to lung over-inflation which may cause adverse cardiopulmonary function or air leak. This was found to be not a significant problem during HFOV in premature infants in experienced centres.20

The early HIFI study was disappointing while more recent studies yielded more favourable results suggested that experience is a very important element in the safe and efficient use of HFV. During HFV important pulmonary parameters such as distal airway pressure, delivered oscillated volume, and inhomogeneities in alveolar ventilation cannot be quantitatively surveyed. No single objective parameter can replace the clinical assessment by an experienced neonatologist.

Sakai et al21 reported 6 cases of pulmonary interstitial emphysema (PIE) in 14 infants treated with Humming 2 ventilator. They postulated that the unusually low MAP used might be the main cause of PIE. At low MAP and low compliance, gas cannot be transported into the atelectatic alveoli. This led to an increase in the amplitude of oscillation in the peripheral airways, resulting in over-expansion of the airways and hence airway injury.

A meta-analysis of studies on the association of IVH & PVL with HFV in premature infants with RDS was performed by Clark.22 A significant association was present only when the HIFI study was included, while analysis of the more recent studies without the HIFI study did not show any association. These findings had led Clark to conclude that HFV was not associated with increased occurrence of IVH or PVL.

Another adverse effect of HFV is the noise pollution by the ventilator.23 The noise produced by Infant Star 500 and SensorMedics 3100A were 53 (49-54) and 59 (56-64) dB respectively. These noise levels were lower than the recommended highest level of 85 dB by the Occupational Safety and Health Administration. However we have to be cautious in using HFV in patients receiving amino-glycosides. These infants are recommended not to be exposed to noise levels of greater than 58 dB.

In an animal study using adult cats, both HFJV and HFOV produced similar inflammatory tracheal damage despite differences in airway pressure exposure and humidity in the two techniques.24 Tracheal damage is a well documented complication of HFJV in neonates, but fortunately not described in HFOV.

Impact of HFOV on Other Neonatal Intensive Care Therapies

Extra-corporal Membrane Oxygenation

Retrospective studies suggest that HFV improves gas exchange in infants with severe respiratory failure and hence reduces the need for ECMO. The response rate to HFV appears to be disease-specific. Infants who have homogeneous lung diseases, such as RDS or pneumonia, are more likely to respond more favourably to HFV than those who have more heterogeneous lung disease such as meconium aspiration pneumonia.

Undoubtedly the combination of HFOV with inO has greatly reduced the requirement for ECMO.23 In recent years, the number of active ECMO centres in the United States has declined leading to more long distance transport. There is also a shift in case mix in patients requiring ECMO, which are now mostly performed in paediatric intensive care patients, cardiac patients and patients with congenital diaphragmatic hernia.

Combined Use of HFOV with Liquid Ventilation

Sukumar et al studied the combined use of HFOV with partial liquid ventilation in preterm lambs.26 They found improvement in gas exchange and stabilization of pulmonary and systemic haemodynamics in these animals. However these studies were still very much experimental at present time.

Conclusion

HFOV used with a high lung volume strategy is a safe alternative to CMV and may even be life saving when used as a rescue therapy. It is better than CMV in causing less baro-volutrauma and can be accepted as one of the first line treatment for RDS in premature infants. However it is not without complications. Experience is an important element in the safe and efficient use of HFOV particularly in premature infants.

There are still many uncertainties about the use of HFV. The different types of HFV devices have not been compared with each other nor with other newer modes of CMV. There are very few studies on the potential benefits of HFV in the extremely-low-birth-weight infants who have the greatest risk of developing CLD. The long term risk-benefit ratio for HFV is not well documented. Follow-up studies should
be performed to investigate the long-term survival, lung function, and neurodevelopment of infants who have been treated with HFV in the neonatal period.

References