Review

Pro/con clinical debate: High-frequency oscillatory ventilation is better than conventional ventilation for premature infants

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Abstract

Arguably one of the most important advances in critical care medicine in recent years has been the understanding that mechanical ventilators can impart harm and that lung-protective ventilation strategies can save lives. High-frequency oscillatory ventilation appears ideally suited for lung protection at first glance. Two camps of opinion exist, however, even in neonates where this modality has been most extensively studied. In the present debate, the prevailing arguments from each of those camps are made available for the reader to decide.

Keywords bronchopulmonary dysplasia, high-frequency oscillation, lung injury, mechanical ventilation, respiratory distress, surfactant deficiency

The scenario

A friend calls you just hours after the unexpected birth of his son at 28 weeks gestation. He tells you the neonatologist would like to transfer his child to a center that has the ability to perform high-frequency oscillatory ventilation (HFOV). He requests your advice on the decision.

Pro: Yes, HFOV is better than conventional ventilation for premature infants

Sherry E Courtney, David J Durand and Jeanette M Asselin

Despite recent advances in perinatal and neonatal care, some very low birth weight infants still require prolonged mechanical ventilation. Providing optimal mechanical ventilation is thus an essential part of the care of very low birth weight infants. There is considerable debate, however, about what is 'optimal' mechanical ventilation.

Animal data from the past 20 years clearly support the superiority of HFOV over conventional ventilation (CV) [1–3]. HFOV is synergistic with surfactant [4,5]. Compared with conventional ventilators, HFOV decreases the levels of some inflammatory mediators in tracheal lavage fluid [6,7]. Most importantly, lung injury from chronic lung disease (CLD) is less with HFOV than with CV [1,8].

Data from clinical trials have been less clear, due mainly to the complexities of performing well-controlled ventilator trials in human infants. Many studies have not employed an appropriate lung recruitment strategy with HFOV. Until recently HFOV has been used as only a 'rescue' technique, based largely on

BPD = bronchopulmonary dysplasia; CLD = chronic lung disease; CV = conventional ventilation; HFOV = high-frequency oscillatory ventilation.

concerns about its possible contribution to intraventricular hemorrhage and/or periventricular leucomalacia [9]. However, the concern about whether HFOV use leads to increased intraventricular hemorrhage and periventricular leucomalacia has finally been laid to rest with the recent publication of two large multicenter trials, neither of which showed any increase in these morbidities [10,11].

HFOV may be provided by a variety of ventilators. Importantly, these machines have well-documented and substantial variations in their performance, making it impossible to compare studies that do not use the same high-frequency device [12,13]. The differences in the outcomes of recent trials of HFOV may be largely due to differences in the devices used.

Early use of HFOV employing a lung recruitment strategy has been studied in several recent large clinical trials. Two of these studies – one that employed HFOV using the Infant Star High Frequency Ventilator (Nellcor Puritan Bennett Inc, Carlsbad, CA, USA) [14], and one that employed predominantly the Drager Babylog 8000 (Drager Medizintechnik, Lubeck, Germany) or the SLE 2000HFO (SLE Life Support, South Croydon, Surrey, UK) [11] – found no differences in pulmonary outcome of HFOV-treated infants compared with infants treated with CV.

In contrast, two large studies that employed HFOV provided by the SensorMedics 3100A (SensorMedics Inc, Yorba Linda, CA, USA) found that infants randomized to HFOV had less chronic lung disease compared with infants randomized to CV [10,15]. Infants on HFOV in the trial by Gertsmann *et al*. [15] also required less surfactant, and fewer infants required prolonged oxygen or ventilator support. In followup at a mean age of 6 years, patients in this study who randomized to CV showed worse pulmonary function than children who had been randomized to HFOV [16]. In the trial by Courtney *et al*., which compared HFOV with a sophisticated CV strategy including both continuous tidal volume monitoring to avoid lung injury from volutrauma and protocolized weaning, HFOV infants fared significantly better than CV infants. In this trial, infants on HFOV were extubated, on average, a full week earlier than infants on CV, and had a lower incidence of CLD [10].

Data available to date thus suggest that early use of HFOV, when provided by the SensorMedics 3100A and utilizing an appropriate strategy, can lead to earlier extubation, to a decrease in CLD, and to improved long-term outcome in the very low birth weight infant. We would support the transfer of patients at high risk of needing prolonged ventilation and/or developing CLD to a center that can provide effective HFOV.

Con: No, HFOV is not better than CV for premature infants

Eric C Eichenwald and Ann R Stark

Most infants born at 28 weeks gestation have respiratory failure due to surfactant deficiency and require assisted ventilation. However, lung injury induced by assisted ventilation contributes to the development of bronchopulmonary dysplasia (BPD), an important cause of chronic illness in these infants. Causes of lung injury include the repetitive expansion and collapse of the lungs, and the delivery by conventional mechanical ventilation of relatively large tidal volumes that overdistend airways and airspaces. This suggests that a ventilator strategy that avoids large cyclic changes in lung volume may reduce lung injury [3,17]. The application of HFOV in premature newborns has generated considerable interest because this technique of rapid ventilation with very small tidal volumes might prevent BPD.

In animal models of respiratory distress syndrome, HFOV used with a strategy of optimizing lung inflation improved gas exchange and lung mechanics, promoted more uniform inflation, reduced air leak, and decreased the concentration of inflammatory mediators in the lung, compared with conventional mechanical ventilation [6]. Unfortunately, avoidance of lung injury by HFOV in animal studies has not been replicated in human preterm infants.

In five of the seven randomized trials comparing HFOV with CV performed since replacement pulmonary surfactant became available to treat respiratory distress syndrome, the type of ventilation made no difference in the rate of survival without BPD [11,14,18–20]. Two trials showed a small benefit of HFOV in that outcome [10,15]. One included few of the infants at highest risk and used relatively high ventilator pressures with CV [15]. The other trial, conducted under rigorously controlled conditions, is the only study that has shown a benefit of HFOV in infants at high risk for BPD [10]. In addition to the lack of benefit found in most of the trials, the rates of pulmonary air leak [10,14] and neurologic complications may be higher in infants treated with HFOV [19,20].

Despite the compelling animal data, HFOV has not been clearly shown to be the 'better' mode of mechanical ventilation for preterm infants for at least two reasons. First, most neonatal intensive care units use conventional mechanical ventilation as the routine mode of respiratory support. Thus, clinical teams often are less experienced with HFOV. This may place individual infants at greater risk for inadvertent overdistention of the lungs, for impaired cardiac output, or for increased central venous pressure that might lead to intracranial hemorrhage. Second, the pathogenesis of BPD is complex, and mechanical injury is only one factor. Other factors that contribute to lung injury, such as delivery circumstances, initial resuscitation, and maternal or neonatal infection, may be more important than the mode of mechanical ventilation in the pathogenesis of BPD [21].

In the most experienced centers, HFOV administered according to strict protocols may offer a small pulmonary benefit in infants at high risk for BPD [10]. However, the majority of available evidence does not support this advantage. For most preterm infants with respiratory distress syndrome, appropriate management includes prompt resuscitation at delivery, early administration of exogenous surfactant, and conventional mechanical ventilation with low tidal volumes and reasonable ventilation goals. In general, HFOV should be reserved for infants in whom CV is failing.

Pro's response

Sherry E Courtney, David J Durand and Jeanette M Asselin

We agree with Eichenwald and Stark that those who use HFOV should be experienced with its use. As with any technology, it must be employed correctly to attain the best results.

We do not agree that HFOV should be reserved for infants in whom CV is failing. Using HFOV only for rescue means delaying its use until volutrauma, barotrauma, and oxygen toxicity have already occurred, making any response to HFOV less likely. The most compelling trials of HFOV are those that began HFOV early in the course and continued it until extubation [10,15,22,23]).

Con's response

Eric C Eichenwald and Ann R Stark

We agree that early HFOV administered by experienced clinicians using strict protocols may provide a small pulmonary advantage in some infants. Most trials, however, have shown no advantage over CV, suggesting that pulmonary outcome may be influenced more by factors other than the mode of ventilation. Furthermore, any potential advantage must be weighed against the known risks of neonatal transport, even between tertiary centers. Transported infants have higher risks of death [24,25], of intraventricular hemorrhage [25–27], and of BPD [25] compared with infants treated in their birth hospitals. We thus do not think transport just for the availability of HFOV is justified.

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