Commentary

Pro/con clinical debate: Is high-frequency oscillatory ventilation useful in the management of adult patients with respiratory failure?

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Abstract

In neonatal and pediatric intensive care units, high-frequency oscillatory ventilation (HFOV) has become an increasingly common therapy. This may not have been the case if researchers had not persisted in investigating the therapy after early disappointing clinical trials. Devices capable of providing this therapy to adults have become commercially available relatively recently. However, there are many questions that need to be answered regarding HFOV in adults: Is HFOV in adults superior to conventional mechanical ventilation? Who is the ideal candidate for HFOV? When should it be applied? What is the best technique with which to apply it? When should a patient on HFOV be converted back to conventional ventilation? What is the safety and efficacy of the device? As outlined in the following debate, there are several compelling arguments for and against the use of HFOV at this point in adults.

Keywords acute respiratory failure, critical illness, high-frequency oscillatory ventilation, mechanical ventilation

The scenario

You have been asked to assist in the organization of and equipment purchases for a new large, state of the art, adult intensive care unit. You are encouraged to obtain leading edge equipment that offers the patients the best hope of survival. While ordering mechanical ventilators, you wonder whether it would be useful to have some high-frequency oscillators.

Pro: Yes, HFOV is useful in the management of adult patients with respiratory failure

Jeffrey M Singh and Sangeeta Mehta

Conventional mechanical ventilation (CMV) may contribute to lung injury through a number of mechanisms, including alveolar overdistension and shear-force injury from end-expiratory collapse [1]. Lung-protective ventilation techniques have been successfully applied in clinical trials demonstrating the efficacy of CMV-based strategies limiting overdistension [2] and preventing end-expiratory collapse [3]. Although successful, these CMV-based strategies each addressed only one aspect of lung protection.

HFOV, applied using an open lung approach, may accomplish all the objectives of lung-protective ventilation. During HFOV, a constant mean airway pressure (P_{aw}) is applied during inspiration and expiration, thus avoiding end-inspiratory overdistension, while maintaining end-expiratory alveolar recruitment. By optimizing alveolar recruitment, and thus ventilation perfusion matching, HFOV improves gas exchange and allows reductions in inspired oxygen concentration (FiO_2) to safer levels. In saline-lavaged rabbits, HFOV attenuated the physiological and pathological changes observed to occur with a lung-protective CMV strategy [4].

The majority of clinical trials evaluating HFOV have been conducted in the neonatal population. Published experience

ARDS = acute respiratory distress syndrome; CMV = conventional mechanical ventilation; HFO = high-frequency oscillation; HFOV = high-frequency oscillatory ventilation; PEEP = positive end-expiratory pressure.

with HFOV in adults with acute respiratory distress syndrome (ARDS) is limited to observational studies [5–8] and one randomized, controlled trial (Derdak *et al*., manuscript submitted).

Two prospective observational studies assessed HFOV as rescue therapy in patients with ARDS and severe oxygenation failure [5,6]. Fort *et al*. evaluated the safety and efficacy of HFOV in 17 adults with ARDS failing inverse ratio ventilation (Lung Injury Severity score, 3.8; PaO_2/F_iO_2, 69 mmHg) [5]. These investigators employed a lung volume recruitment strategy targeting $PaO_2 \geq 60$ mmHg and $F_iO_2 \leq 0.6$ mmHg. Mehta *et al*. also evaluated HFOV in 24 patients with ARDS (Lung Injury Severity score, 3.4; PaO_2/FiO_2, 99 mmHg) after varying periods on CMV [6]. To optimize lung recruitment, these investigators applied significantly higher mean airway pressures during HFOV than had been applied previously with CMV.

Both studies observed significant improvements in oxygenation within 8 hours of HFOV initiation, allowing a majority of patients to benefit from a decrease in FiO_2. Ventilation was maintained with HFOV, and there were no adverse events. Despite higher mean airway pressures, there were no clinically significant hemodynamic sequelae. Interestingly, both studies noted that survivors had been ventilated with CMV for fewer days before institution of HFOV compared with non-survivors, suggesting potential benefit to early use of HFOV in the support of patients with ARDS.

Two additional smaller observational studies have described the safe use of HFOV in burns and trauma patients [7,8], and demonstrated similar improvements in oxygenation with HFOV. In one of these studies, HFOV was used during anesthesia and surgery, allowing surgery to proceed in burns patients who may otherwise have been too unstable to go to the operating room [7].

Derdak *et al*. have recently concluded a prospective, multicenter, randomized trial comparing HFOV with CMV in 148 adults with ARDS (manuscript submitted). The HFOV group showed significant early improvement in oxygenation compared with the CMV group. Patients randomized to HFOV had a trend to decreased 30-day mortality compared with patients on CMV (37% versus 52%). There were no differences between the two groups in hemodynamic variables, failure of oxygenation or ventilation, or barotrauma.

HFOV, by allowing the safe use of high mean airway pressures, may satisfy all of the objectives of lung-protective ventilation. HFOV has been shown to be safe and effective at improving gas exchange and reducing FiO_2 requirements for adults with ARDS. The early use of HFOV, perhaps by mitigating ventilator-induced lung injury, may be advantageous.

Con: No, HFOV is not useful in the management of adult patients with respiratory failure

Robert M Kacmarek

It is unnecessary for a new, large, state of the art, adult intense care unit to use HFOV. There is no data to indicate that the survival of adult patients with ARDS is improved with the use of HFOV.

Animal data

Most of the studies published over the past 40 years comparing HFOV with CMV have favored HFOV [9]. In almost all of these studies, however, HFOV is compared with CMV in ways that, today, we know to be a lung-injurious ventilatory pattern [1]. That is, CMV was provided with a large tidal volume (V_T) and low positive end-expiratory pressure (PEEP), while HFOV was applied with an open lung, protective approach to ventilation.

A number of studies have recently been performed with both HFOV and CMV using a similar open lung approach to ventilation [4,10,11]. In two of these studies [10,11], no differences on any variable assessed existed between the two approaches. In the most recent study [4], however, HFOV resulted in less inflammatory and histologic injury than CMV. Lung recruitment maneuvers were used prior to setting PEEP in the two studies showing no differences between HFOV and CMV [10,11], whereas in the Imai *et al*. study [4] no recruitment was performed and PEEP was arbitrarily set during CMV at 8–10 cmH_2O.

Neonatal data

At least 11 randomized, controlled trials of high-frequency ventilation in infants have been performed, with nine of these trials using HFOV [12]. The overall results of these trials are equivocal. In a meta-analysis, Thome and Carlo [12] indicate there is no difference in mortality between the use of HFOV and CMV. Although HFOV results in less chronic lung disease (i.e. the need for oxygen at 30 days of life), this finding is confounded by the fact that the three largest HFOV trials found no difference in the incidence of chronic lung disease. Thome and Carlo also found increased incidence of severe intracranial hemorrhage and periventricular leukomalasia during HFOV. They go on to state that HFOV cannot be recommended for routine use and that there is limited data suggesting benefit during rescue use of HFOV over CMV. It must be pointed out that, in all of these trials, CMV was applied with low PEEP (≤ 5 cmH_2O), whereas HFOV was primarily applied with an open lung approach.

Adult data

There are no published randomized comparisons of HFOV with CMV in the management of adult acute respiratory failure. Two case series have been published [5,6]; however, the data from these trials raise concerns regarding lung protection during HFOV. In both series, mean airway

pressures up to 45 cmH_2O were set with pressure amplitudes as high as 90 cmH_2O, resulting in peak alveolar pressures exceeding 50 cmH_2O. In addition, low rates (3–5 Hz) were needed to maintain ventilation. It can be argued that, at these low rates, V_T approaches those values recommended during CMV [13]. Overall mortality of these trials is high (59% [6] and 67% [5]), although the authors describe the trials as rescue trials.

Conclusion

When considering the recent data from the ARDSnet trial [14] demonstrating low mortality (31%), using a lung-protective protocol in a large heterogeneous group of acute lung injury/ARDS patients, and considering the lack of definitive data demonstrating improved outcome with HFOV in neonates, it is impossible to recommend HFOV as standard or even rescue care in the management of any adult patient.

Pro's response: All CMV is not created equal

Jeffrey M Singh and Sangeeta Mehta

Dr Kacmarek refers to animal studies showing similar outcomes to high-frequency oscillation (HFO) when CMV is applied with an open lung approach. However, the utility of these animal studies in guiding the practical management of patients with severe hypoxemia is limited by the need for pressure–volume curve measurements [11] and the use of respiratory frequencies of 150 bpm [10] during CMV.

Although tidal volumes and alveolar pressures during HFOV have not been measured, HFOV has been shown to have a comparable safety profile with CMV in adults with ARDS (Derdak *et al*., manuscript submitted). Until a trial comparing HFOV with the best available lung-protective CMV strategy is complete, the existing evidence supports the benefit and safety of HFOV as rescue therapy in patients with ARDS.

Con's response: HFO must be proved better than ARDSnet!

Robert M Kacmarek

Dr Singh and Dr Mehta have referred to the unpublished HFO trial (Derdak *et al*., manuscript submitted), indicating that the mortality of the HFO group was 37% and that of the conventional ventilation group 52%. This difference was not significant but, more importantly, the approach to conventional ventilation must be questioned. What were the V_T values used and what were the end-inspiratory plateau pressures in this trial? My understanding is that the V_T values were 9–10 ml/kg and the plateau pressures were >30 cmH_2O. If this is true, it is difficult to consider this trial as an endorsement for HFO. We know from the ARDSnet trial [14] that small V_T values (4–6 ml/kg) and plateau pressure <30 cmH_2O resulted in a 31% mortality. Before we can embrace HFO, it must be compared with our 'best' method of applying conventional ventilation.

Competing interests

JMS and SM work in the intensive care unit of the Mount Sinai Hospital in Toronto, Canada, which has received the "3100B high frequency oscillatory ventilator", together with technical support, from the company, SensorMedics.

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