

Editorial II

High-frequency oscillation in acute respiratory distress syndrome (ARDS)

Over the past 15 years, the mortality associated with acute respiratory distress syndrome (ARDS) has steadily declined. In the late 1980s and early 1990s, 33% of patients with the syndrome survived to leave hospital, compared with survival rates of 60–75% reported more recently.^{1–3} Although the explanation for this reduction is likely to be multifactorial, improvements in ventilation techniques have undoubtedly made a major contribution.

Current best-practice with regard to ventilation in ARDS is often described as ‘protective’ ventilation or the ‘open-lung’ approach, and involves recruitment manoeuvres to re-expand atelectatic areas of lung, followed by application of relatively high levels of positive end-expiratory pressure (PEEP) to prevent airway closure and alveolar collapse at end-expiration (atelectrauma). In addition, tidal volumes are limited to 6 ml kg⁻¹ and plateau pressure to <30 cm H₂O to avoid overdistension of the lung at end-inspiration (volutrauma).⁴ When this approach is followed, pulmonary and systemic cytokine levels are minimized and further biotrauma avoided.⁵ Two large studies have confirmed that this high PEEP, low tidal volume strategy reduces mortality in ARDS, and Amato’s results also show that it is associated with significantly less barotrauma.^{6,7} Since the widespread adoption of protective ventilation, cases of severe barotrauma, such as the one reported by Galvin in this issue of the Journal,⁸ have fortunately become relatively uncommon. Nevertheless, as this case demonstrates, when they do occur they present a difficult management problem.

The case raises a number of questions with regard to the use of high-frequency oscillation in ARDS: what is the rationale behind the use of high-frequency oscillation ventilation (HFOV) in ARDS; is there any evidence to support its use as a rescue therapy when conventional ventilation is failing or from the outset; and does it reduce the incidence of air leaks or have a role in treating them?

Theoretically, HFOV has a number of advantages over conventional ventilation in ARDS. In this regard, it may be helpful to think of HFOV as an extreme form of standard protective ventilation, that uses sub-deadspace tidal volumes (1–3 ml kg⁻¹) and significantly higher levels of PEEP (equal to the continuous distending pressure or mean airway pressure during HFOV). These two features reduce the risk of cyclical alveolar collapse and over-distension, an important factor in the genesis of ventilator-induced lung injury (VILI). If similar tidal volumes and levels of PEEP were applied at conventional frequencies (<50 bpm), carbon dioxide clearance would be compromised. However, during HFOV, the

use of higher frequencies (180–360 bpm or 3–6 Hz) enables arterial carbon dioxide levels to be maintained within normal limits. At the lower end of the frequency range (3 Hz), carbon dioxide clearance is usually better because of the larger tidal volume generated. Higher proximal driving pressures (range 60–90 cm H₂O) and longer inspiratory times (range 30–50%) will also enhance carbon dioxide clearance through a similar effect on tidal volume.⁹ The ability to maintain a higher mean airway pressure, whilst keeping plateau pressure <30 cm H₂O, is a further advantage over conventional ventilation, and one that improves oxygenation and allows the inspired oxygen concentration to be reduced. Novel mechanisms of gas exchange that come into play or assume greater importance during HFOV may also contribute to better oxygenation and carbon dioxide removal. Bulk convection and diffusion are the predominant mechanisms of gas exchange during conventional ventilation, whereas interregional gas mixing between units with different time constants (Pendelluft), convective transport attributable to asymmetry between inspiratory and expiratory velocity profiles, and longitudinal dispersion owing to interaction between the axial velocity profile and radial concentration gradient (Taylor’s dispersion), also play a significant role during HFOV.^{10–12}

Clinicians are now faced with the challenge of translating the theoretical advantages of HFOV in ARDS into a demonstrable effect on clinical outcome.

Early studies by Fort¹³ and Mehta,¹⁴ and more recently Matthias,¹⁵ focused on the use of HFOV as a rescue therapy, with patients being placed on HFOV only when conventional ventilation was observed to be failing. Although these studies were small (*n*=17–42), uncontrolled, and therefore unable to demonstrate any conclusive outcome benefit, they did show that mean airway pressure could be safely maintained at a higher level with HFOV and oxygenation (P/F ratio, oxygenation index (OI)) improved. A number of other consistent themes emerged, including that prolonged conventional ventilation before institution of HFOV was associated with a poor outcome. In Mehta’s study, survivors received conventional ventilation for a mean of 1.6 vs 7.8 days for non-survivors (*P*=0.001),¹⁴ and in Matthias’ study the mortality for patients who had received conventional ventilation for >3 days was 64 vs 43% for the group as a whole.¹⁵ Fort also demonstrated that patients with the worst oxygenation at baseline (OI>47) had a greater risk of dying.¹³

The logical progression from this work was to undertake a randomized, controlled study of HFOV vs best conventional ventilation, aiming to randomize patients at an early stage in

their illness to avoid prolonged and potentially deleterious periods of conventional ventilation before the institution of HFOV. Derdak and colleagues¹⁶ undertook this study, enrolling 148 patients in 13 North American centres between October 1997 and December 2000. With regard to the case reported in this issue of the Journal,⁸ it should be noted that patients with more than one intercostal catheter per hemithorax and an air leak for >120 h were excluded from the study, as were patients who had been ventilated with >80% oxygen for >48 h.

In interpreting the results of his study, it is important to remember that the design of the best conventional limb predated publication of both Amato's⁵ and the ARDS Network⁶ papers. In the conventional treatment algorithm, target tidal volume was 6 ml kg⁻¹, based on actual rather than ideal body weight, and the mean tidal volume delivered was in fact 8 ml kg⁻¹. Limits were not specified for either plateau or peak airway pressure, and extubation was not protocolized. Thus the conventional limb is not representative of our current best practice. It is also important to note that recruitment manoeuvres only formed part of the protocol in the HFOV treatment limb, and thus patients in the conventional limb may have been deprived of the beneficial relationship between P_{aO_2} and mean airway pressure observed on the deflation vs inflation limb of the pressure-volume curve. The transition from HFOV back to conventional ventilation at relatively high levels of inspired oxygen ($F_{iO_2}=0.5$) and mean airway pressure (24 cm H₂O) may conversely have adversely affected outcome in the HFOV group.

Overall, P/F ratio was significantly better in the first 16 h in the HFOV group, with OI at 16 h being the best predictor of survival. Factors linked to poor outcome included: >5 days of conventional ventilation before randomization; APACHE 2 score; OI at 16 h; and baseline pH. Mortality at 30 days and 6 months was lower in the HFOV group (37 vs 52% and 47 vs 59%, respectively), although neither result reached a *P*-value of <0.05. Therefore, despite the conceptual advantages of HFOV and a trend towards lower mortality in the HFOV group, this study failed to conclusively prove that HFOV was superior to conventional ventilation in ARDS.

When considering the issue of air leaks, there is no evidence in the adult literature to suggest that the incidence of new or worsening air leaks is higher during HFOV than conventional ventilation. In the HFOV limb of Derdak's study the incidence was 9 vs 12% in the control group, whilst the rescue studies reported rates of 3–8%. An early study in premature neonates (the HIFI study) did document higher rates of air leak specifically pneumoperitoneum of pulmonary origin in the HFOV group, but the design of this study has been criticised for employing a low-volume strategy and applying HFOV late.¹⁷ Subsequent studies in neonates and paediatric patients comparing HFOV and conventional ventilation have reported similar rates of air leak with the two techniques.^{18–22}

Once an air leak has developed, HFOV may reduce the size of the leak and promote healing of the lung through several mechanisms. By avoiding high peak airway pressures, the alveolar-pleural pressure gradient is reduced and the driving pressure for gas to move through the site of the leak is minimized. High peak airway pressures will also increase the physical size of the leak, whereas the short inspiratory times and small tidal volumes used during HFOV help reduce the diameter of the leak. With this reduction in diameter, resistance to gas flow through the leak is increased and healing of the lung facilitated. Although there are a number of case reports in the paediatric literature of HFOV being used as a rescue therapy to manage cases of pneumonia complicated by severe air leak, Galvin is one of the first to document this management approach in an adult.^{8 23 24} Furthermore, it seems unlikely that a randomized controlled study to compare HFOV and conventional ventilation in the management of severe air leak will ever be undertaken, given the declining incidence of barotrauma since the introduction of the 'open lung' approach. With limited adult data available to guide our use of HFOV in severe air leaks, it may be useful to consider some of the conclusions from Ellsbery's work in a neonatal pig model of experimental pneumothorax.²⁵ In this model, he observed that gas flow through the air leak could be minimized by setting the oscillator at a relatively high frequency, with a low percentage inspiratory time (30 or 33% rather than 50%), low proximal distending pressure, and low mean airway pressure. Changes in mean airway pressure were also noted to result in the greatest percentage change in the size of the air leak. This implies that efforts to reduce mean airway pressure should take precedence over alterations in the other parameters wherever feasible. In my experience, it is also essential to incorporate brief intermittent recruitment manoeuvres into this strategy, so that by working on the deflation limb of the P-V curve the lowest possible mean airway pressure is used to achieve a given P_{aO_2} .

In conclusion, HFOV is equal to conventional mechanical ventilation from the outset in patients with ARDS. It is also useful as a rescue therapy for refractory hypoxaemia or ventilatory failure, and in the management of severe air leaks. Previous studies comparing HFOV and conventional ventilation in adults with ARDS have been compromised by the inability to maintain spontaneously breathing adults on HFOV. Patients randomized to HFOV have therefore received a combination of HFOV and conventional ventilation. If the oscillator can be modified to meet the inspiratory flow requirements of the spontaneously breathing adult, a further study comparing HFOV as the sole mode of ventilation with best conventional ventilation at that time should be undertaken.

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Editorial III

Remembering awareness[†]

This edition of the *British Journal of Anaesthesia* includes abstracts from the Sixth International Symposium on Memory and Awareness in Anaesthesia, which was held in Hull during June 2004. These symposia have a distinguished pedigree going back to the 1980s when Dr Benno Bonke joined

with Professor Keith Millar and Dr William Fitch to plan the First International Symposium on Memory and Awareness,

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