〔特別講演〕

The Role of High Frequency Oscillatory Ventilation (HFOV) and Extracorporeal Membrane Oxygenation (ECMO) in the Support of Neonates with Respiratory Failure

Robert A. deLemos*

Introduction

The term "high frequency ventilation (HFV)" refers to a group of ventilatory techniques which share in common the use of lower than normal tidal volume and supraphysiologic respiratory frequencies. The innovative aspect of these approaches is the use of tidal volumes near to, or less than, dead space volume. The high frequencies serve merely as a vehicle to allow the use of low tidal volumes.

Although extensive research has looked into gas transport under these conditions, the differences between gas exchange during HFV and conventional mechanical ventilation appear to qualitative. Both bulk and diffusive flow appear to play a role although their relative contributions during HFV may be different.

Classification of HFV techniques is also controversial. Froese has suggested that they be grouped according to the mode of exhalation[1]. There are HFV systems in which exhalation is passive and dependent solely on the mechanical properties of the lung and other systems in which a negative pressure gradient between the lung and proximal airway is actively created during exhalation. This enhances gas egress and reduces gas trapping. As a result, it appears that the "active" exhalation ventilators (such as oscillators) can be safely operated at higher frequencies and lower volumes than those in which exhalation is passive (jet ventilators and flow interrupters).

Oscillatory ventilators are one form of active exhalation high frequency ventilator. Using either a piston, diaphragm or bellows, a nearly equal volume of gas is injected and withdrawn in each ventilatory cycle. Since this results in no net gas delivery to the patient, a source of fresh gas must be introduced proximal to the piston. Regulation of the bias flow rate and a resistance on the exhalation limb determine the mean airway pressure. Tidal volume can be regulated independently.

Use of HFOV in the treatment of hyaline membrane disease

In spite of substantial progress in the management of premature infants with hyaline membrane disease over the past ten years, bronchopulmonary dysplasia (BPD) remains a major complication of ventilator and oxygen management of premature infants. Although the precise etiology of BPD is unknown, most investigators feel that pulmonary baroinjury and oxygen toxicity are major contributing factors.

* Department of Physiology and Medicine, Southwest Foundation for Biomedical Research, San Antonio, Texas, 78284, USA

During HFOV, the intrapulmonary intraluminal pressure amplitude is significantly reduced compared to conventional mechanical ventilation (CMV). Thus one can use the same or higher mean airway pressure ($\overline{P}_{aw}$) with substantially lower peak airway pressure. Since oxygenation in diffuse alveolar disease is related to $\overline{P}_{aw}$, this theoretically would allow for optimal oxygenation at a reduced risk of barotrauma.

We compared HFOV to CMV in premature baboons with hyaline membrane disease[2]. The animals were delivered at 140 days gestation and initially placed on positive pressure ventilation with positive end expiratory pressure (PPV/PEEP). After a 3 hour instrumentation/stabilization period, animals were randomized either to HFOV or PPV/PEEP. During HFOV frequency was kept at 10 Hz with an I : E ratio of 1 : 2. Oxygenation was optimized by adjustment of the mean airway pressure in both groups of animals.

In the PPV/PEEP animals, F_{IO_2} and Pa/A O_2 changed little over the first 20 hours (**Fig. 1**). $\overline{P}_{aw}$ had to be increased to maintain oxygenation within protocol guidelines. The HFOV animals started on a higher $\overline{P}_{aw}$ after randomization. There was a dramatic fall in F_{IO_2} and rise in Pa/A O_2 immediately after institution of HFOV. These finding reached significance by 20 hours. None of the HFOV animals developed clinical, radiographic, or morphologic evidence of airleak. In contrast, 55 percent of the PPV/PEEP animals developed pulmonary interstitial emphysema (PIE), pseudocyst, or pneumothorax.

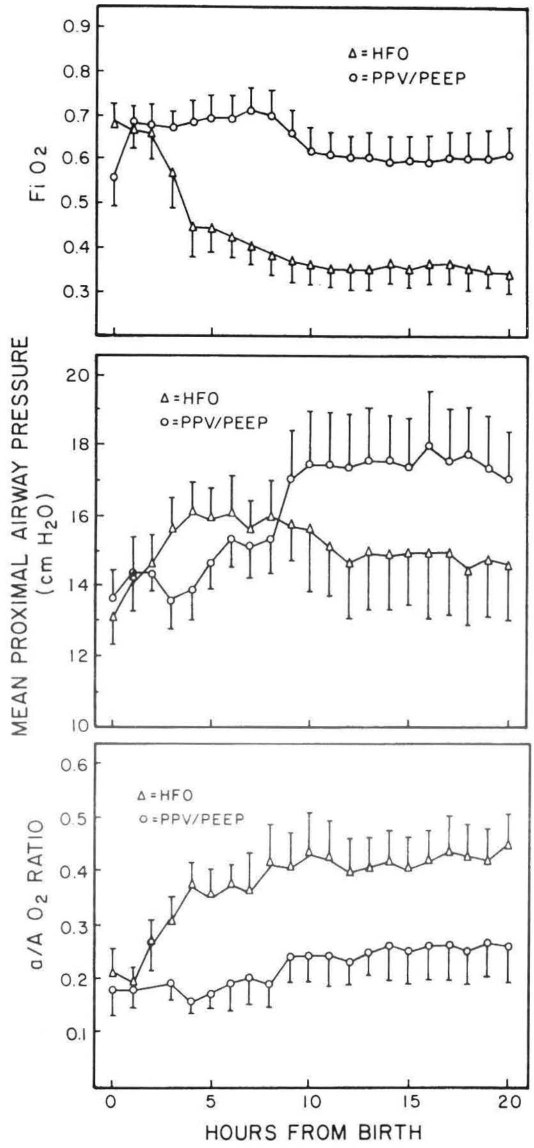

Fig. 1 F_{IO_2}, mean airway pressure, and a/AO_2 ratio over the first 20 h in premature baboons treated with HFOV compared with those treated with PPV/PEEP. Note the rapid improvement in oxygenation after beginning HFOV

These data showed that the use of HFOV in premature animals with hyaline membrane disease resulted in dramatic improvement in oxygenation. Even though higher $\overline{P}_{aw}$ was used with HFOV than with PPV/PEEP this resulted in significantly less pulmonary barotrauma. Thus HFOV reduced both oxygen exposure and baroinjury in this model.

We have now managed over 100 infants with hyaline membrane disease and pulmonary hypoplasia with HFOV. In most cases the human experience is similar to that seen in the nonhuman primate experiments. In particular, the clinical course of infants with pulmonary hypoplasia from diaphragmatic hernia has been markedly improved with HFOV management. These findings suggest that many aspects of the " natural history " of HMD and pulmonary hypoplasia may in fact result from ventilator-induced pulmonary barotrauma. They further suggest that HFOV is indicated in the management of these and other pulmonary conditions where the presence of diffuse alveolar disease places the patient at high risk for barotrauma.

Use of HFOV in the management of airleak

Because it can be used to achieve adequate ventilation and oxygenation at lower intraluminal peak distending pressures, HFOV has been shown to be advantageous in the management of patients with pulmonary interstitial emphysema and pneumothorax.

If the patients can be managed with intrapulmonary pressures below those forcing gas through the leak, the magnitude of the air leak will diminish and the tissue will heal.

We have used HFOV in the management of over 100 infants with PIE and intractable respiratory failure. Overall more than 70% of patients meeting these criteria have survived after treatment with HFOV. Survival, however, appears dependent on the severity of the airleak prior to institution of high frequency ventilation[3]. When chest radiographs are graded from " mild " (grade 1) to " severe " (grade 3) PIE, survival is 100% when infants are placed on HFOV at grades 1 and 2, and only 60% when the disease has progressed to grade 3. This indicates that HFOV should be instituted as early as possible in this condition.

In general we have used frequencies between 10 and 15 Hz in management of infants with airleak. As in uncomplicated HMD, the $\overline{P}_{aw}$ is the determinant of oxygenation. However, when airleak is present we use a lower mean pressure and accept a higher F_{IO_2}. Tidal volume determines ventilation at any frequency. Extreme caution must be taken to insure that the frequency selected dose not result in inadvertent air trapping when treating infants with airleak with HFV.

Use of Extracorporeal Membrane Oxygenation (ECMO) in the management of infants with intractable hypoxemia and/or respiratory failure

This technique was adapted from short term cardiopulmonary bypass by Kolobow and others and until recently was used in only a few medical centers. However, in the past 2 years there has been increased interest and use of ECMOin the management of infants with severe pulmonary disease.

The ECMO system consists of a patient circle and four key elements : (1) low pressure sensor, (2) rotary pump, (3) membrane oxygenator, and (4) heat exchanger (**Fig. 2**). At the present time, no manufacturer makes all elements of the system and parts must be acquired from as many as 20 distributors.

The most common mode of vascular access is veno-arterial. Cannulae are inserted surgically into the right atrium (via the jugular vein) and carotid artery. Blood is removed via the vein and reinfused into the aorta. The route allows near-total cardiac support. Its major limitations are the requirement for systemic heparinization and the need to ligate the carotid artery at the conclusion of the procedure.

Veno-venous bypass has been attempted either by use of two veins or a " single needle " technique. These routes can be used only for partial support and, at the present time, re-

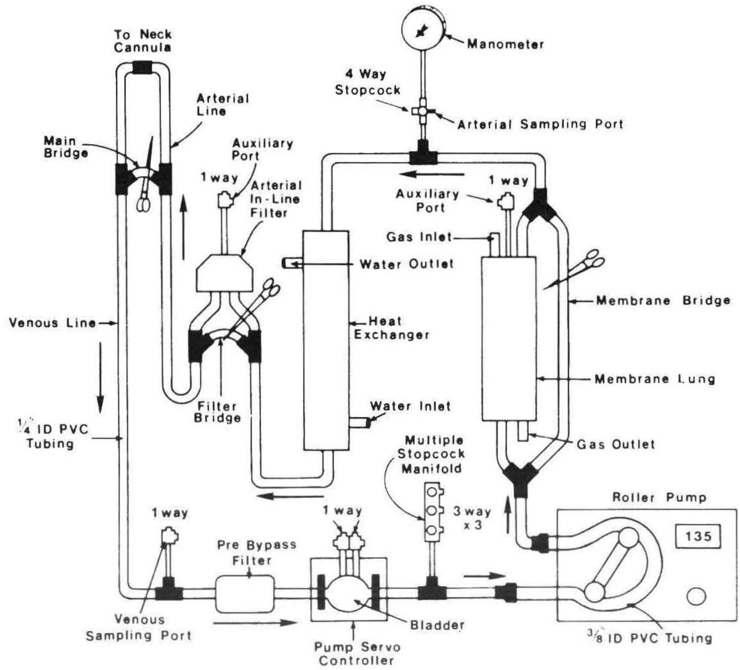

Fig. 2 Schematic diagram of ECMO circuit

quire systemic heparinization. Since many infants requiring ECMO have severe cardiac dysfunction and may require total bypass, this approach has limited applicability in neonates.

The generally accepted criteria for the use of ECMO therapy include : (1) birth weight over 2 kg, (2) age of 7 days or less, (3) evidence of severe pulmonary disease (A-aDo$_2$>600, pH<7.15, Pao_2>55) or cardiovascular decompensation, and (4) the absence of severe lethal underlying disease or malformations. The presence of prematurity is an absolute contraindication for ECMO because of the risks of periventricular hemorrhage with systemic heparin therapy and the problems of catheter size and resistance. The restrictions based on age are predicated on the assumption that, after 7 days of age, lung disease would not be reversible within the time constraints of ECMO use. This clearly is not applicable in the case of older children and adults and does not apply when new ventilatory strategies, such as HFOV, are used in conjunction with ECMO. In the latter case, many infants previously excluded from ECMO use have been successfully treated.

Major complications of ECMO include : bleeding diatheses, ulcers, seizures, stroke, and various mechanical problems related to the system. There are no adequate follow-up data defining the long-term risks of either the technique itself or carotid ligation.

The combined use of ECMO and HFOV

We have used both ECMO and HFOV in the management of infants with intractable respiratory failure. In the years 1985-86, 50 infants were referred to Wilford Hall USAF Medical Center for ECMO therapy. All met the criteria listed above. With the exception of two infants who were placed on bypass at the referring hospital and air-transported on ECMO, all were initially begun on HFOV. Twenty-eight never went onto bypass. Twenty-three of these survived ; five died before cardiac bypass could be established. Eighteen of 22 infants going on ECMO survived. The overall survival was 82% and was identical in both groups.

HFOV was used to maintain lung volume and provide some ventilation during ECMO. This allowed for reduced pump flow rates and permitted earlier decannulation of many patients. Infants who could not be supported with conventional mechanical ventilation after bypass were successfully managed with HFOV.

Thus, the combined use of HFOV and ECMO appears from preliminary data to offer certain advantages over either technique alone. Many infants meeting standard ECMO criteria can be managed with HFOV alone, thus avoiding the risks of heparinization and carotid ligation. The lungs can be maintained above closing volume during bypass, without risk of additive baroinjury. Lastly, the use of HFOV allows decannulation of many infants who could not otherwise be removed from bypass.

Conclusions

Both HFOV and ECMO appear to have roles in the management of infants with severe respiratory failure. They also have potential applicability in the management of adults with similar types of pulmonary disease. Both of these techniques are in an early state of development and additional research will be necessary to define the optimal strategy for their use.

References

1. Froese AB and Bryan AC : High frequency ventilation. Am Rev Respir Dis 135 : 1363, 1987
2. deLemos RA, Coalson JJ, Gerstmann DR, et al : Ventilatory management of infant baboons with hyaline membrane disease ; The use of high frequency ventilation. Pediatr Res 21 : 594-602, 1987
3. Clark RH, Gerstmann DR, Null DM Jr, et al : Pulmonary interstitial emphysema treated by high-frequency oscillatory ventilation. Crit Care Med 14 : 926-930, 1986