A protocol for high-frequency oscillatory ventilation in adults: Results from a roundtable discussion*

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Objective: Ventilator settings typically used for high-frequency oscillatory ventilation (HFO) in adults provide acceptable gas exchange but may not take best advantage of its lung-protective aspects. We provide guidelines for HFO in adults with acute respiratory distress syndrome that should optimize the lung-protective characteristics of this ventilation mode.

Design: Roundtable discussions, iterative revisions, and consensus.

Setting: Five academic medical centers.

Patients: Not applicable.

Interventions: Participants addressed how to best maintain ventilation through combinations of oscillation pressure amplitude, frequency, and the use of an endotracheal tube cuff leak, and to maintain oxygenation through combinations of recruitment maneuvers, mean airway pressure, and oxygen concentration. The guiding principles were to provide lung protective ventilation by minimizing the size of tidal volumes, and balance the risks and benefits of lung recruitment and distension.

Main Results: HFO may provide smaller tidal volumes and more complete lung recruitment than conventional modes. To optimize these features, we recommend use of the maximum pressure-oscillation amplitude coupled with the highest tolerated frequency, targeting a pH of only 7.25–7.35. This will yield a smaller tidal volume than typical HFO settings where frequency is limited to 6 Hz or less and pressure amplitude is submaximal. Lung recruitment can be achieved with the use of recruitment maneuvers, especially during the first several days of HFO. Recruitment may be augmented or sustained with generous mean airway pressures. These may either be chosen from a table of recommended mean airway pressure and oxygen concentration combinations, or individually titrated based on the oxygenation response of each patient.

Conclusions: Modification of the goals and tactics of HFO use may better protect against ventilator-associated lung injury. Further clinical trials are needed to compare the effects on patient outcome of the best use of HFO compared to the most protective use of conventional modes in adult acute respiratory distress syndrome. (Crit Care Med 2007; 35:1649–1654)

KEY WORDS: mechanical ventilation; high-frequency ventilation; protocols; acute respiratory distress syndrome; acute lung injury; ventilator-associated lung injury; acute respiratory failure

High frequency oscillatory ventilation (HFO) has been widely used to ventilate neonatal and pediatric patients for more than 2 decades. Only recently, HFO has become available for support of adults weighing more than 35 kg with acute lung injury or acute respiratory distress syndrome (ARDS). HFO utilizes a relatively high mean airway pressure (mPaw). This may sustain lung recruitment more effectively than levels of positive end-expiratory pressure that are typically used during conventional ventilation. HFO also uses tidal volumes that are smaller than those used with conventional ventilation. These features may protect against ventilator-induced lung injury (VILI) more effectively than lung-protective strategies with conventional modes of mechanical ventilation (1–3).

HFO settings recommended in the user's manual (4) and used in clinical studies (5–7) have been developed largely by trial and error, based on their ability to provide acceptable gas exchange in most patients. However, these settings may not represent the most lung-protective use of HFO. Studies of lung-protective approaches to conventional ventilation have shown that ventilator settings that improve gas exchange may not reduce mortality; indeed, the opposite may occur (8). If HFO is to improve patient outcome from acute lung injury or ARDS, it is essential that it be used in a manner that minimizes VILI, rather than a manner that merely normalizes arterial blood gases.

When used with currently recommended settings (4), HFO tidal volumes may be only slightly smaller than those used during lung-protective conventional ventilation, according to preclinical data (9,

10). Furthermore, mPaw during HFO often is set at levels that are considered dangerous plateau pressures during conventional ventilation. Methodology to improve the lung-protective aspects of HFO would attempt to further reduce tidal volume and give careful consideration to the relative risks of higher mPaw vs. higher F_{IO_2}.

Therefore, we convened a roundtable discussion of several researchers and clinicians who were experienced in the use of HFO. Our goal was to reach consensus on an approach to HFO that we thought would maximize its lung protective virtues while maintaining acceptable gas exchange and safety. Discussion was limited to use of the SensorMedics 3100B ventilator (Viasys Healthcare, Yorba Linda, CA), the only HFO ventilator currently approved for adult use in the United States. The use of expert opinion was considered necessary because few of the details about HFO settings have been subjected to study in adults with ARDS. Furthermore, the lack of surrogate end points that correlate with mortality make such studies exceedingly challenging. This consensus approach to the use of HFO is offered as a guide for clinical use of this new technology, until this or other approaches can be tested directly in clinical trials.

METHODS

The co-authors were contacted to request their consultative advice regarding the optimal use of HFO. Participants were from the United States and Canada, and were selected based on their record of publication, participation, and planning of other clinical studies of HFO. An additional participant (BTT) was invited specifically because he is *not* experienced with HFO, but has extensive experience in clinical trials of lung-protective mechanical ventilation. He was asked to act as an impartial moderator. The final participant (DH) acted as recording secretary, providing written summaries of the proceedings.

A series of five, weekly, 1.5-hr conference calls was held during July-August 2005. Before the series of calls, we circulated a draft protocol for HFO, together with a draft agenda and a request for input. After initial feedback was incorporated, we divided the protocol into a series of issues for discussion in each conference call. Following each conference call, the content was summarized in writing and was circulated for correction or comment. One participant from each institution (NF, SD, RK, RB) acted as a voting member, and votes on specific issues were recorded. Votes and open issues were reviewed at the beginning of each subsequent conference call. We then circulated a draft version of the completed consensus protocol for comment and revision. This paper reports the final version of that document, adapted to be more suitable for routine clinical use with input from all authors.

Results are presented in the form of an outline to facilitate bedside use or institutional protocol development. Although the authors agreed on most issues, we could not reach consensus on the approach to oxygenation. For this aspect of HFO management, two alternative approaches are provided and the rationale for each is presented in the Discussion.

RESULTS

Metarules

1. HFO may be considered for patients with ARDS who are failing conventional ventilation, as defined below. In the absence of studies showing improved clinical outcomes, HFO remains investigational for routine management of ARDS.
2. Ventilation should target pH 7.25–7.35. Attempts to raise pH to the normal range will require larger tidal volumes, potentially promoting more VILI.
3. Ventilation goals are achieved using frequency as the primary adjustment, rather than the oscillation pressure amplitude. Higher frequencies are emphasized, which will result in smaller and potentially less injurious tidal volumes.
4. Oxygenation should target Sp_{O_2} 88–95% or Pa_{O_2} 55–80 mm Hg. Setting an upper limit of tolerable oxygenation will minimize potential adverse effects of excess oxygen or mPaw.
5. Initial settings and adjustments are performed rapidly, with adjustments for oxygenation goals as frequently as every 5 mins. Thereafter, ventilator adjustments (except for dangerous hypoxemia) are made no more frequently than every 2 hrs to assure a steady state.
6. We suggest two distinct alternative approaches to oxygenation management. One (approach A) places somewhat less emphasis on lung-recruitment maneuvers and provides a table of mPaw and F_{IO_2} combinations to simplify bedside application. The other (approach B) favors more aggressive lung recruitment and attempts to individualize mPaw and F_{IO_2} combinations for each patient based on their oxygenation response. These approaches represent differing views of the benefits and risks of recruitment maneuvers and associated high airway pressure, as well as differing philosophies on the design and application of bedside protocols, which could not be reconciled.

Protocol

1. Usual indications for HFO.
   a. Oxygenation failure: $F_{IO_2} \geq 0.7$ and positive end-expiratory pressure >14 cm H_2O or
   b. Ventilation failure: pH <7.25 with tidal volume ≥ 6 mL/kg predicted body weight and plateau airway pressure ≥ 30 cm H_2O.
2. Usual contraindications to HFO.
   a. Known severe air flow obstruction.
   b. Intracranial hypertension.
3. Initial HFO settings.
   a. Bias flow = 40 L/min.
   b. Inspiratory time = 33%.
   c. mPaw = 34 cm H_2O.
   d. F_{IO_2} = 1.0.
   e. Amplitude (ΔP) = 90 cm H_2O.
   f. Initial frequency based on most recent arterial blood gas:
      i. pH <7.10 = 4 Hz.
      ii. pH 7.10–7.19 = 5 Hz.
      iii. pH 7.20–7.35 = 6 Hz.
      iv. pH >7.35 = 7 Hz.
   g. After initial HFO settings a) through f) are established, perform an initial recruitment maneuver and oxygen/mPaw adjustment as described below (see 4, below).

Management of Oxygenation—Approach A, F_{IO_2}/mPaw Table

4. Initial recruitment maneuver (RM) and mPaw/oxygen titration.
   a. Assure adequate vascular volume.
   b. Set high mPaw alarm to 55 cm H_2O.
   c. Turn off piston.
   d. Raise mPaw to 45 cm H_2O over 10 secs.

Table 1. Recruitment maneuver (RM) precautions

1. Do not perform recruitment maneuvers in patients with hypotension or pneumothorax and active air leak.
2. Terminate a recruitment maneuver immediately if associated with hypotension (mean arterial pressure <60 mm Hg or decrease by >20 mm Hg) or desaturation (decrease in oxygen saturation to less than 85% or decrease of more than 5%).
3. Do not repeat recruitment maneuvers for at least 24 hours in patients in whom previous RM had to be terminated, as above.

Table 2. Mean airway pressure (mPaw) and inspired oxygen (F_{IO_2}) combinations: mPaw is to be set ±1 cm H_2O of target value.

Step	F_{IO_2}	mPaw (cm H_2O)
1	0.4	22
2	0.4	24
3	0.5	24
4	0.5	26
5	0.5	28
6	0.5	30
7	0.6	30
8	0.6	32
9	0.7	32
10	0.7	34
11	0.8	34
12	0.8	36
13	0.8	38
14	0.9	38
15	1.0	38
16	1.0	40
17	1.0	42[a]
18	1.0	45[a]

[a]Steps 17 and 18 are optional. Consider the use of neuromuscular blockade, prone positioning, or other adjuvant therapies in patients requiring this level of oxygenation support. Small (±5 cm H_2O) fluctuations in association with respiratory efforts are allowable; larger fluctuations suggest the need for deeper sedation.

e. Maintain 45 cm H_2O for 45 secs (see Table 1, Cautions).
f. Reduce mPaw to 34 cm H_2O.
g. Reset high mPaw alarm to 40 cm H_2O.
h. Resume piston oscillations at $\Delta P = 90$ cm H_2O and observe for 10 mins.
i. If oxygenation < goal range, repeat RM but raise mPaw to 50 cm H_2O (see Table 1, Cautions) then reduce mPaw to 36 cm H_2O.
j. If oxygenation > goal range, decrease F_{IO_2} by 0.05 every 5 mins until Spo_2 88–95%.
k. Observe for 4 hrs. Increase F_{IO_2} if necessary during this period for oxygenation < goal range persisting >5 mins.

l. If after 4 hrs:
   i. Oxygenation > goal range, decrease F_{IO_2} and/or mPaw at intervals of 2 hrs to match nearest combination in Table 2.
   ii. Oxygenation < goal range, increase F_{IO_2} and/or mPaw every 5 mins to match nearest combination in Table 2.
   iii. Oxygenation in goal range, adjust F_{IO_2} and mPaw either up or down as necessary at intervals of 2 hrs to match nearest combination in Table 2.
5. Subsequent adjustments for oxygenation (approach A).
   a. Make subsequent adjustments in F_{IO_2} and mPaw according to Table 2. Changes can be made every 5 mins for oxygenation < goal range; no more frequently than every 2 hrs for oxygenation > goal range.
   b. Conduct RMs under the following conditions:
      i. During days 1–5 of HFO, immediately preceding any increase in mPaw required by the protocol above 25 cm H_2O.
      ii. During any day of HFO, if oxygenation falls < goal range after a manipulation likely to cause derecruitment (e.g., suctioning, airway disconnection, repositioning, agitation).
   c. Perform RM as follows:
      i. Remove cuff leak, if present.
      ii. Increase F_{IO_2} to 1.0.
      iii. Follow steps 4a) through 4e) as per initial RM.
      iv. Return mPaw and F_{IO_2} to pre-RM settings (if RM was for derecruitment) or to higher step from Table 2 (if RM was for hypoxemia). Restore cuff leak, if applicable.

   v. Return ΔP to 90 cm H_2O and reset mPaw alarms for 5 cm H_2O above and below mPaw.

Management of Oxygenation—Approach B, F_{IO_2}/mPaw Titration Without Table

6. As in approach A, subsequent adjustments for oxygenation follow steps 4a) through 4j) for initial settings and RMs. Thereafter:
   a. Once Spo_2 or Pao_2 is in goal range, decrease mPaw 2 cm H_2O every 15 mins until Spo_2 <88%.
   b. Repeat RM as per steps 4a) through 4e).
   c. Return mPaw to the level preceding the RM +2 cm H_2O.
   d. Return F_{IO_2} to the level preceding RM as identified in step 4i).
   e. As oxygenation improves (Spo_2 or Pao_2 > goal range), decrease F_{IO_2} in 0.05–0.1 steps until $F_{IO_2} = 0.4$.
   f. When $F_{IO_2} = 0.4$, decrease mPaw in 2 cm H_2O steps every 4–6 hrs, provided the Spo_2 is >88% or Pao_2 >55 mm Hg, until the mPaw is 22 cm H_2O.
   g. If Spo_2 falls to <88% for >5 mins, repeat RM and reset mPaw to 2 cm H_2O above level preceding RM.
   h. After 5 days of HFO, RMs for Spo_2 <88% should only be performed if the patient continues to respond (increase in Spo_2 by ≥5% within 5 mins).
   i. In the patient who does not increase Spo_2 (or Pao_2) with a RM, increase F_{IO_2} in 0.05–0.1 steps if necessary to meet oxygenation goal. Once $F_{IO_2} = 1.0$, increase mPaw in 2 cm H_2O steps if necessary to meet oxygenation goal.

Subsequent Adjustments

7. Subsequent adjustments for ventilation; goal is pH 7.25–7.35 at highest achievable frequency.
   a. If pH >7.35:
      i. Increase f by 1 Hz every 2 hrs until pH is in goal range or $f = 15$ Hz.

ii. If f = 15 Hz, then decrease ΔP by 5–10 cm H_2O every 1–2 hrs.
   b. If pH <7.25:
      i. If ΔP <90 cm H_2O, increase ΔP in increments of 5–10 cm H_2O every 1–2 hrs until pH is in goal range or to maximum of 90 cm H_2O.
      ii. If ΔP = 90 cm H_2O, decrease f by 1 Hz every 2 hrs until pH is in goal range or f = 3 Hz.
   c. If a f ≥7 Hz cannot be achieved within 4 hrs, institute 5 cm H_2O cuff leak.
      i. Suction oropharynx.
      ii. Set pressure alarms to 55 and 10 cm H_2O.
      iii. Increase bias flow until mPaw increases by 5 cm H_2O.
      iv. Slowly deflate endotracheal tube cuff until mPaw falls by 5 cm H_2O to its previous level.
      v. Return pressure alarms to settings preceding cuff leak.
   d. If pH <7.25 on f = 4 Hz, bronchoscopically inspect airway for mucus accumulation, endotracheal tube kink, or malposition.
   e. If pH <7.10 on f = 3 Hz, remove inline suction catheter and recheck arterial blood gases within 1 hr.
   f. If pH remains <7.10, bicarbonate infusion may be given.
8. Sedation and neuromuscular blockade.
   a. Patients should be deeply sedated at the onset of HFO.
   b. Suggested regimen is a combination of a benzodiazepine and narcotic.
   c. Propofol may be added to avoid very high doses of benzodiazepine and narcotic.
   d. Neuromuscular blockade may be given as intermittent boluses while titrating sedatives to suppress respiratory effort.
   e. If continuous neuromuscular blockade is used, it should be stopped once daily to assess the need for its continued use.
   f. Small respiratory efforts that alter mPaw by <±5 cm H_2O do

not require further suppression unless oxygenation or ventilation are compromised.
9. General care.
   a. Once HFO is initiated, patients should remain on it for a minimum of 12 hrs.
   b. Elevate head of bed ≥30 degrees unless otherwise contraindicated.
   c. Use a heated humidifier, not a heat-moisture exchanger.
   d. Use inline suction catheter to avoid airway disconnections during suctioning.
   e. If disconnection is needed, remove cuff leak (if present) and clamp endotracheal tube with padded clamp to avoid derecruitment.
   f. Auscultate heart and abdomen briefly with HFO piston off but without disconnection. If necessary, auscultate lungs during manual bagging.
   g. Check ventilator hourly until oxygenation and ventilation are within goal, per routine thereafter.
   h. Document frequency, bias flow, mPaw, F_{IO_2}, ΔP, and power setting with ventilator checks.
10. Transition to conventional ventilation.
   a. Convert to conventional ventilation when patients have reached step 1 of Table 2 (using approach A) or mPaw = 24 cm H_2O (approach B) and remained on those settings for at least 12 hrs.
   b. Initial settings:
      i. Vt = 6 mL/kg predicted body weight.
      ii. F_{IO_2} = 0.5.
      iii. Positive end-expiratory pressure = 16 cm H_2O.
      iv. RR = 25.
   c. Check arterial blood gas in 30–60 mins.
   d. Adjust settings and continue small tidal volume, lung-protective conventional mechanical ventilation until recovery and weaning.
   e. Revert back to HFO if patient again meets criteria for oxygenation or ventilation failure (section 1).

DISCUSSION

There have been few randomized trials comparing HFO to conventional ventilation in adults, and all were too small to detect differences in important clinical outcomes (5, 7). Furthermore, HFO technology is relatively new and remains unfamiliar to many clinicians. It requires rental or purchase of a ventilator that has no use other than support of patients with acute lung injury or ARDS. These factors—unfamiliarity, expense, and the lack of a solid body of evidence—hamper the wide use of HFO.

We have proposed approaches to HFO that emphasize its potential to minimize the injurious stresses that can exacerbate lung injury (11). These approaches use the smallest tidal volume that can maintain acceptable CO_2 clearance, and use relatively high mPaw to attempt to recruit lungs and avoid repetitive airway opening and closure. These are the principles that make HFO attractive as a lung-protective ventilator mode. However, our specific suggestions differ in some important respects from the instructions in the SensorMedics 3100B user manual (4) or methods described in some case series and trials of HFO in adults (5–7, 12, 13).

First, we have not targeted a pH in the normal range. This is based on the rationale that modest degrees of acidosis are well-tolerated in most patients, and were allowed in the largest randomized trial of HFO in adults (5). Furthermore, efforts to normalize the pH would require either larger or more frequent breaths, which would be undesirable, as our goal is to prioritize lung protection. Thus, a pH of only 7.25–7.35 is suggested.

Second, we recommend achieving that pH at a frequency that is higher than has generally been used in adults, and at a ΔP of 90 cm H_2O, the maximum that can be reached in most adult patients. This approach will result in smaller tidal volume, despite the high ΔP setting, than those that would be achieved at lower frequencies and ΔP. Unlike conventional ventilation, tidal volume and respiratory rate are not independent during HFO. As frequency increases in HFO, inspiratory time decreases, and therefore tidal volume does, too. This inverse dependence of tidal volume on frequency during pressure-cycled HFO has been shown in mechanical model (10, 14), animal (9), and human (15) studies. For $Paco_2$ to remain constant, alveolar ventilation must be

constant. Therefore, at any target Pa_{CO_2}, tidal volume must be smaller at higher frequencies, even if ΔP has been increased. Consequently, we recommend frequency as the primary adjustment for pH (and Pa_{CO_2}) rather than ΔP (which is left on its maximal setting of 90 cm H_2O).

Although there is little published experience ventilating adults at these high frequencies [16], it is within the capabilities of the ventilator. Similar high frequencies are used routinely in pediatrics and neonatology [17, 18]. In our experience, most adults with severe ARDS can maintain adequate ventilation at frequencies higher than 5 Hz [19]. It remains unknown whether decreasing tidal volume below its already small values at 5 Hz during HFO will reduce VILI, or whether benefits of still smaller tidal volumes are offset by their greater frequency. One recent study compared HFO at 5 Hz and 15 Hz in saline-lavage–injured rabbits, with ΔP adjusted to provide identical gas exchange [20]. Animals ventilated at 15 Hz showed lower tissue neutrophil scores after 4 hrs, although other indices of histologic injury were similar.

Third, we provide two approaches to the management of oxygenation, an area in which we could not reach general consensus. One approach (A) utilizes a uniform initial mPaw of 34 cm H_2O in all patients, in contrast to the usual recommendation of 5 cm H_2O above the mPaw during conventional ventilation. This approach has been adopted from the ARDS Network trials [8]. The initial high mPaw emphasizes early lung recruitment. It has been our experience that the standard recommendation (mPaw 5 cm H_2O above the mPaw on conventional ventilation) is often insufficient to allow substantial reduction of F_{IO_2} when patients with severe ARDS are first placed on HFO. We base subsequent adjustments on a table of fixed, recommended mPaw and F_{IO_2} combinations. The use of the table provides consistency, transparency, and reproducibility to the application of HFO. It allows ventilator adjustments to be made by therapists, house staff, or others less familiar with the technology. The specific combinations were selected after intensive discussion in an attempt to balance the risks and benefits of high fractions of inspired oxygen and high mean airway pressure. These risks include oxygen toxicity and mechanical risks of lung overdistension or circulatory depression from high mPaw, or recruitment/derecruit-

ment injury from low mPaw [21]. Although we believe these combinations of F_{IO_2} and mPaw will be suitable for most patients, as always, there will be exceptions. Clinical expertise will be required to recognize when another approach is needed.

The alternative approach to oxygenation (B) attempts to individualize F_{IO_2} and mPaw adjustments, using the improvement in oxygenation as a marker for optimal lung recruitment. The use of a decremental mPaw titration is based on the work of Hickling [22], with the goal of setting the lowest mPaw on the deflation limb of the pressure-volume curve of the respiratory system that will maintain an improvement in oxygenation achieved by a successful RM [23]. After finding this initial setting of mPaw, the mPaw is held constant as gas exchange improves until the F_{IO_2} requirement is minimal (0.4). The goal of this approach is to maintain a highly recruited lung volume until lung recovery begins, at which point mPaw is slowly decreased. Mean airway pressure is set based on the oxygenation of each patient, used as a surrogate for their respiratory system mechanics. This approach places somewhat lower emphasis on the risks of elevated airway pressures, and minimizes the risks of prolonged high F_{IO_2} compared to the use of a mPaw/F_{IO_2} table. However, it does require a greater amount of time initially at the bedside titrating these settings. This approach also makes some untested assumptions about how lung recruitment is reflected by oxygenation.

Fourth, we have recommended relatively frequent recruitment maneuvers. These, too, carry both potential risk and benefit. The potential benefit is that RMs may more rapidly or effectively recruit the lung. Lung recruitment has been demonstrated following RMs in animal [24] and human studies that have used pressures up to 60 cm H_2O [6, 25, 26]. Effective recruitment may allow reduction in mPaw due to the hysteresis of the lung pressure-volume relationship. However, RM-induced recruitment often varies with the mechanism and stage of lung injury [27–29], and may not be sustained [29–31]. Potential risks of RMs include transient hypotension or desaturation [31], or barotrauma. They also add complexity to the routine clinical use of HFO. As is the case with mPaw, risks and benefits of RMs are unquantified. Our approach uses RMs more frequently early in the course of HFO, and after manipula-

tions likely to result in derecruitment. Even without RMs, HFO utilizes mean airway pressures that are substantially greater than during conventional ventilation and may achieve more lung recruitment [32]. More research is needed to clarify the risks, benefits, and optimal methods for RMs.

Our consensus process has limitations. We did not utilize a formal consensus development method, such as the Delphi or Nominal Group Process. These are unsuitable for the myriad specific decisions needed to develop a detailed protocol. We assembled a limited number of participants. These likely do not represent the full range of opinions about HFO, and are only a few of the experienced users of this technology. However, the participants represented several North American institutions with significant HFO and clinical trials experience, and knowledge and experience with VILI. Agendas and materials for discussion were circulated in advance, contributing to the transparency of the consensus process. To avoid domination by any one institutional bias or personality, each participating center had one vote, and a nonvoting and nonpartisan moderator was chosen.

CONCLUSION

Current literature supports HFO use in adults to attempt to improve gas exchange in patients failing conventional ventilation [5–7, 13, 33, 34]. Other benefits, particularly survival outcomes, await testing in adequately powered trials. Early routine use of HFO for adults with ARDS therefore cannot be recommended outside of an investigational setting.

However, for either investigational or rescue use, we believe the technical approach suggested here will support gas exchange while optimizing the potential lung protective characteristics of HFO. It is hoped that this provides a logical, systematic, and practical approach to HFO that takes best advantage of its potential to minimize VILI. Whether that potential actually improves patient outcomes awaits the findings from future trials.

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