High-Frequency Ventilation: State-of-the art 2010

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Disclosures

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Dr. Keszler is a consultant to Draeger Inc. He has, in the past, received research support and honoraria for lectures.

FDA:

Various approved high frequency and conventional vents will be discussed.
HIGH FREQUENCY VENTILATION

- **Definition:** A group of ventilatory techniques that utilize supra-physiologic rates and small tidal volumes

- **Rationale:** To reduce pressure/volume related injury to lung parenchyma, decrease the risk of airleak and chronic lung disease, and to facilitate the resolution of existing airleak.
AIRWAY PRESSURE WAVEFORMS

HFOV

HFJV
## Characteristics of HFV devices

<table>
<thead>
<tr>
<th></th>
<th>HFOV</th>
<th>HFJV</th>
<th>HFFI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF pulses generated by:</td>
<td>Piston or other means</td>
<td>Pinch valve, Injector cannula</td>
<td>Solenoid valve</td>
</tr>
<tr>
<td>I : E ratio</td>
<td>1: 1 or 1: 2</td>
<td>1: 4 to 1: 8</td>
<td>1: 3 to 1: 6</td>
</tr>
<tr>
<td>Opt. Freq.</td>
<td>8 to 15 Hz</td>
<td>5 to 10 Hz</td>
<td>8 to 12 Hz</td>
</tr>
<tr>
<td>Ability to superimpose a sigh</td>
<td>No (SM) Yes (Babylog)</td>
<td>Yes (able to interrupt HF or not)</td>
<td>Yes (with interruption of HFV)</td>
</tr>
<tr>
<td>Waveform</td>
<td><img src="image" alt="Waveform" /></td>
<td><img src="image" alt="Waveform" /></td>
<td><img src="image" alt="Waveform" /></td>
</tr>
</tbody>
</table>
Oscillator
High-Frequency Jet Ventilator
Jet Streaming & Coaxial Flow

Coaxial flow pattern with simultaneous inhalation and exhalation
Gas exchange during HFV

Classical respiratory physiology:

Alveolar ventilation \((V_a) = V_t - V_d \times \text{rate}\)

\[\text{If } V_t \leq V_d\]

then \(V_a = 0 \times \text{rate} = 0 (!)\)
Gas-Transport Mechanisms during HFOV

Convection zone

Direct Ventilation of close alveoli

Turbulence in large airways

Turbulent flow with radial mixing

Pendelluft

Expiratory symmetrical velocity profiles

Inspiratory asymmetrical velocity profiles (laminar flow)

Convection & diffusion zone

Diffusion zone

Spike Convection & Facilitated Diffusion during HFV

1) SLOW

2) FAST

3) VERY FAST

4) STOP
Eliminating CO\textsubscript{2}

CV → \dot{V}_{CO_2} \propto f, V_T

HFV → \dot{V}_{CO_2} \propto f, V_T^2
Principles of gas exchange

**Oxygenation:**

- Efficiency depends on optimizing V/Q matching.
- V/Q matching is a function of maintaining optimal lung volume.
- Lung volume is proportional to Paw.
- Oxygenation is possible without ventilation.
PaO₂ as a function of mean airway pressure after either deflation from total lung capacity or inflation from relaxation volume in saline-lavaged rabbits.

PV Relationship in NB on HFOV

Tingay, et al 2005
HFV: High rate, low $V_T$, low $\Delta P$

Low $V_T$ and $\Delta P$ makes it possible to use high PEEP without high PIP. Ventilation on the expiratory limb of the P-V loop, once recruitment occurs.
Different Ways to Achieve Lung Recruitment

Polglase, et al,

J. Appl Physiol 2008
Lung Recruitment: Effects on PBF

Clinical use of HFV

- **Late rescue**
  - Infants failing conventional ventilation
  - Widely accepted
  - High morbidity and mortality

- **Early rescue**
  - Infants at high risk of complications
  - Generally accepted

- **First-line treatment**
  - Promising, physiologically attractive
  - Still controversial
<table>
<thead>
<tr>
<th>Author</th>
<th>Model</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>deLemos '87</td>
<td>Baboon</td>
<td>HFOV decreases lung injury, increases expansion</td>
</tr>
<tr>
<td>Meredith '89</td>
<td>Baboon</td>
<td>HFOV improves gas exchange, decreases histologic changes</td>
</tr>
<tr>
<td>Kinsella '91</td>
<td>Baboon</td>
<td>HFOV improves oxygenation</td>
</tr>
<tr>
<td>Jackson '91</td>
<td>Monkey</td>
<td>HFOV improves gas exchange, decreases edema</td>
</tr>
<tr>
<td>Suzuki '92</td>
<td>Rabbit</td>
<td>HFOV decreases lung injury</td>
</tr>
<tr>
<td>Froese '93</td>
<td>Rabbit</td>
<td>Hi vol strategy improves surf effect</td>
</tr>
<tr>
<td>Jackson '94</td>
<td>Monkey</td>
<td>HFOV and surfactant synergistic</td>
</tr>
</tbody>
</table>
Reduction in Lung Injury with Combined Surfactant and HFOV

(Jackson J.C. et al. 1994)

Figure 4. Oxygenation index, radiograph score, lung injury score, and volume fraction of alveolar debris at 6 h (see Figure 3 and text for definitions). **p 0.0001 (compared with HFOV+SURF). *p < 0.015 (compared with HFOV+SURF).
Can HFV Prevent BPD?

- Premature baboons (125/185 days)
  - prenatal steroids
  - surfactant
- Randomized to HFOV or IMV by 5 min
- Followed for 28 days
  - HFOV group had better lung mechanics
  - HFOV group had better lung pathology

Ventilator Induced Lung Injury

Chronic Changes

Lung biopsy at 7 mo
- 40% reduction of tissue volume with CV
- formation of fewer alveolar crests with CV
- “alveolar simplification”
Established Indications for HFV

- Pulmonary interstitial emphysema\(^1\)
- Pneumothorax/broncho-pleural fistula\(^2\)
- Severe respiratory failure refractory to CV\(^3\)
- Chest/abdominal wall restriction\(^4\)
- Pulmonary Hypoplasia (anecdotal)
- Adjunct to iNO \(^5\)

\(^1\) Keszler, J Ped ’91; \(^2\) Gonzales, J Ped ‘87; \(^3\) Clark, J Ped ’94; \(^4\) Keszler, Ped Res ’97; Fok, Arch Dis Child ’97; \(^5\) Kinsella J Ped ‘97
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Condition</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hi Fi ‘89</td>
<td>673</td>
<td>RDS, 750-2000</td>
<td>HFOV did not lower CLD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1100g)</td>
<td>Incr. IVH, low BP, Ptx, X-over</td>
</tr>
<tr>
<td>Carlo ‘90</td>
<td>42</td>
<td>RDS, 1-2 kg</td>
<td>HFJV did not lower CLD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1420g)</td>
<td>Incidence of IVH same</td>
</tr>
<tr>
<td>Keszler ‘91</td>
<td>144</td>
<td>PIE, &gt;750</td>
<td>HFJV accelerated resolution of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1336g)</td>
<td>PIE Incidence of IVH same</td>
</tr>
<tr>
<td>Clark ‘92</td>
<td>83</td>
<td>RDS, &lt;1750</td>
<td>HFOV reduced CLD.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1100g)</td>
<td>Incidence of IVH same</td>
</tr>
<tr>
<td>HiFO ‘93</td>
<td>176</td>
<td>Severe RDS &gt;500</td>
<td>HFOV reduced new airleak</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1700g)</td>
<td>IVH slightly higher</td>
</tr>
<tr>
<td>Ogawa ‘93</td>
<td>92</td>
<td>RDS, 750-2000</td>
<td>HFOV did not improve outcome.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1200g)</td>
<td>Incidence of IVH same</td>
</tr>
</tbody>
</table>
### HFV in RDS Clinical Trials II

**Surfactant era, pre-PTV**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Condition</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerstmann '95</td>
<td>125</td>
<td>RDS, &lt;35wk (1500g)</td>
<td>HFJV did not improve CLD. Incidence of IVH/PVL increased. Higher risk of IVH/PVL or death.</td>
</tr>
<tr>
<td>Wiswell '96</td>
<td>73</td>
<td>RDS, &lt;33wk, &gt;500g (945g)</td>
<td>HFOV incr. surv. w/o CLD, decreased cost. Incidence of IVH/PVL same</td>
</tr>
<tr>
<td>Keszler ‘97</td>
<td>130</td>
<td>RDS, 750-1500 (1020g)</td>
<td>HFJV reduced CLD, home O2. Incidence of IVH/PVL same overall, lower with Optimal Volume Strategy.</td>
</tr>
</tbody>
</table>
HFJV vs. CMV in Uncomplicated RDS

- Multicenter randomized clinical trial
- HFJV vs. CV in RDS
- Early intervention, post-surfactant
- Primary outcome measure: CLD @ 36 wk
- Early termination 2° Wiswell’s study and FDA – generated delay
- Some deviation from designated optimal volume strategy: post-hoc analysis
Major Pulmonary Outcomes

- Home O2
- BPD@36wk
- Airleak

CV: p<0.05
HFJV: p<0.01

PVL / Grade 3-4 IVH


p = 0.04 for HF - OPT vs. HF - LOW
PaCO₂ (torr)

Time (h)

HF-OPT  HF-LO  CV

P < 0.05
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Description</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plavka ‘99</td>
<td>43</td>
<td>RDS, 500 - 1500g (836 g)</td>
<td>HFOV (Sensormedics) reduced CLD at 28 and 36 wks. IVH, PVL same</td>
</tr>
<tr>
<td>Thome ‘99</td>
<td>284</td>
<td>RDS, 24-30 wks, (880 g)</td>
<td>HFFI did not improve outcome. HFFI Increased airleak</td>
</tr>
<tr>
<td>Moriette ‘01</td>
<td>273</td>
<td>RDS, 24-29 weeks (986 g)</td>
<td>HFOV (Dufour 1:1 ratio) did not improve pulmonary outcome. Increased IVH, low PCO2</td>
</tr>
<tr>
<td>NVSG ‘02</td>
<td>498</td>
<td>601-1200g, &lt; 4 h (855 g)</td>
<td>HFOV (Sensormedics) led to faster extubation, incr. survival w/o BPD</td>
</tr>
<tr>
<td>UKOS ‘02</td>
<td>797</td>
<td>23-28 wk, &lt; 1h (853 g)</td>
<td>No difference in pulmonary or neurologic outcome (HFOV-SLE) Some Sensormedics and Draeger</td>
</tr>
</tbody>
</table>
The NSVG Multicenter Trial
Survival without CLD

CV  HFOV

0% 10% 20% 30% 40% 50% 60% 70% 80%

601-700 701-800 801-1000 1001-1200
Figure 2. Kaplan–Meier Curves Showing Ages at Which Infants Were Successfully Extubated. The curves are significantly different (P=0.006 by the Cox proportional-hazards estimate; hazard ratio, 0.76 [95 percent confidence interval, 0.62 to 0.92]). The vertical lines show the age at which 50 percent of the infants assigned to each group were successfully extubated.
UKOS study, NEJM, Aug 2002

- Survived
- CLD
- Alive w/o CLD

- CV 23-25 wk
- HFOV 23-25 wk
- CV 26-28 wk
- HFOV 26-28 wk
## NVSG vs. UKOS

<table>
<thead>
<tr>
<th></th>
<th>NVSG</th>
<th>UKOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study entry</td>
<td>&lt; 4 hrs</td>
<td>&lt; 1 hr</td>
</tr>
<tr>
<td>Eligibility</td>
<td>601-1200 g</td>
<td>23-28 wks</td>
</tr>
<tr>
<td>Severity of RDS</td>
<td>MAP &gt;6, FiO₉ &gt;0.25</td>
<td>All included</td>
</tr>
<tr>
<td>HFOV strategy</td>
<td>Optimal volume</td>
<td>Optimal volume</td>
</tr>
<tr>
<td>CV strategy</td>
<td>Well defined</td>
<td>Not defined</td>
</tr>
<tr>
<td>Device</td>
<td>SensorMedics, 1:2</td>
<td>SLE 2000, 1:1 ratio</td>
</tr>
<tr>
<td>Weaning</td>
<td>On assigned mode for 2 wk or extubation.</td>
<td>Changed to CV early to wean</td>
</tr>
</tbody>
</table>
Importance of I:E Ratio in HFOV

- 1 day old piglets
- Alveolar vs endotracheal pressures
  - ETT clamp technique
- Infrasonics, Babylog 800, SensorMedics
- With 50% $T_{\text{insp}}$: $P_{\text{alv}} > P_{\text{ETT}}$
- With shorter $T_{\text{insp}}$: $P_{\text{alv}} < P_{\text{ETT}}$

_Thome, J Appl Physiol 84:1520, ‘98_
### HFV in RDS Clinical Trials IV

**Surfactant ERA, Gentle PTV**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Patient Details</th>
<th>Outcome Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Reempts ‘03</td>
<td>300</td>
<td>RDS, &lt;32 wk, &lt; 6 h. (1195 g)</td>
<td>Pulmonary &amp; neurologic outcome same. (Sensormedics / Infant Star)</td>
</tr>
<tr>
<td>Craft ‘03</td>
<td>46</td>
<td>RDS, &lt;1000 g</td>
<td>No difference in BPD or IVH, trend to more airleak (HFFI)</td>
</tr>
<tr>
<td>Schreiber ‘03</td>
<td>207</td>
<td>RDS, &lt;34 wk, &lt; 2000 g</td>
<td>No difference in BPD or IVH (Sensormedics HFOV +/-iNO)</td>
</tr>
<tr>
<td>Vento ‘05</td>
<td>40</td>
<td>RDS, &lt;1500 g &lt; 29 wk</td>
<td>HFOV (Draeger) vs. SIMV decreased BPD @ 36 wk. Neuro outcome same</td>
</tr>
<tr>
<td>Dani ‘05</td>
<td>25</td>
<td>BW = 1126 g, GA = 28.3 wk</td>
<td>HFOV (Sensormedics) + opt vol. vs. PSV+VG low vol. reduced pro-inflammatory Cytokines</td>
</tr>
<tr>
<td>Lista ‘08</td>
<td>40</td>
<td>BW = 1010 g GA = 27.4</td>
<td>HFOV (Draeger) + opt vol. vs. AC+VG + opt vol. increased pro-inflammatory Cytokines</td>
</tr>
</tbody>
</table>
Cumulative Meta-analysis
(van Vught 2003)
Conclusions

- There are important device differences.
- There are key strategy differences.
- There are major population differences in:
  - Size and maturity
  - Rate of antenatal steroid use
- Most studies did not define CMV strategy.
- “Successful” studies compared optimal volume HFOV with low volume CMV.
Concerns re. HFV as first-line treatment in infants with uncomplicated RDS?

- Lingering concern over safety.
- Improvements in CV technology (PTV).
- Advent of volume-targeted ventilation
Arguments in favor of CV

- Importance of monitoring $V_T$
- Avoidance of hypocarbia
- Value of synchronization
- Less hemodynamic impairment (?)
- Less noise, vibration, handling
- Fewer chest radiographs
- Ease of handling, positioning, kangaroo care
- Auto-weaning strategies
Open Lung Concept with CMV

- Following surfactant therapy, HFOV was not better than CMV with the open lung strategy in improving gas exchange, lung deflation stability and in the prevention of lung injury. This indicates that **achieving and maintaining alveolar expansion (i.e. open lung) is of more importance than the type of ventilator used.**

  Gommers, et al, Eur Respir J., 1999
OLC Prevents Lung Injury
Conclusion

- HFV and State-of-the-Art CV are converging approaches.
- HFV remains an important tool in the treatment of respiratory failure.
- Optimal use of available equipment with attention to the underlying pathophysiology is more important than which machine is employed.
- The Open Lung concept protects against VILI, regardless of which frequency is used. Don’t be afraid to use adequate PEEP.