HFOV IN THE NON-RECRUITABLE LUNG

PPHN
Pulmonary hypoplasia after PPROM
Congenital diaphragmatic hernia
Pulmonary interstitial emphysema / cystic lung disease
APPROACH TO TREATMENT OF PPHN

- Confirmation of the diagnosis (clinical + ECHO)
- Treatment for the underlying lung disease
  - Ventilatory support
  - ± Exogenous surfactant
  - ± Antibiotics
- Circulatory support
- Adjunctive treatment for PPHN
- Definitive treatment for PPHN
Circulatory support and adjunctive therapy in PPHN

**Circulatory support**
- Increasing systemic BP may reduce R→L shunt through the ductus arteriosus
- Possible agents: dobutamine ± noradrenaline or milrinone
- Avoid agents that reduce systemic blood pressure (e.g. tolazoline)
- Do not volume overload

**Adjunctive therapy**
- Heavy sedation and muscle relaxation until stable
- Correction of:
  - Hypoglycaemia
  - Hypocalcaemia
  - Hypomagnesemia
  - Polycythaemia or anaemia

Fluid bolus
→ increased systemic blood pressure
→ decreased R to L ductal shunt
Ventilatory support in PPHN

- Most infants with significant PPHN benefit from intubation and ventilation
- Should apply ventilation so as to:
  - Achieve normocapnia and pH 7.35-7.45
  - Optimise lung volume and avoid ventilator-induced lung injury
- FRC (end-expiratory lung volume) is an important determinant of pulmonary blood flow
- For parenchymal disease + PPHN, high frequency ventilation is recommended, as FRC may remain poor on conventional ventilation
- For pulmonary hypoplasia + PPHN, high frequency ventilation is recommended, as overdistension and/or ventilator-induced lung injury worsen PPHN
- For “idiopathic” PPHN, conventional ventilation is preferred

Relationship between lung volume and PVR

Simmons Circ Res 1961
Ventilatory support in PPHN

Relationship between lung volume and PVR

Simmons Circ Res 1961

Recruitment manoeuvre to 28 cm H$_2$O → higher PVR → oxygenation worse
Post-recruitment
→ oxygenation better at same P_{aw}
→ pre-post ductal difference less


HFOV and iNO in PPHN
HFOV and iNO in hypoxic respiratory failure in PICU

Dobyns et al Crit Care Med 2002

Bay 2 Pulmonary hypoplasia
Preterm infants with extreme PPROM
RWH Melbourne 2001-2005

Membrane rupture <24 weeks
Minimal latent period 14 days

Table 3 Infants who died in the neonatal unit

<table>
<thead>
<tr>
<th>Birth weight (g)</th>
<th>Gestational age at rupture of membranes (completed weeks)</th>
<th>Latent period (days)</th>
<th>Cord pH</th>
<th>Nitric oxide</th>
<th>Pneumothorax</th>
<th>Age at death</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 730</td>
<td>21</td>
<td>29</td>
<td>–</td>
<td>No</td>
<td>Yes</td>
<td>&lt;1 h</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td>2 730</td>
<td>22</td>
<td>31</td>
<td>–</td>
<td>No</td>
<td>Yes</td>
<td>72 h</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td>3 1606</td>
<td>23</td>
<td>71</td>
<td>7.22</td>
<td>No</td>
<td>Yes</td>
<td>56 h</td>
<td>Respiratory failure</td>
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<tr>
<td>4 655</td>
<td>19</td>
<td>33</td>
<td>7.10</td>
<td>No</td>
<td>No</td>
<td>&lt;1 h</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td>5 850</td>
<td>18</td>
<td>56</td>
<td>–</td>
<td>No</td>
<td>Yes</td>
<td>&lt;1 h</td>
<td>Respiratory failure</td>
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<tr>
<td>6 720</td>
<td>18</td>
<td>59</td>
<td>7.21</td>
<td>No</td>
<td>Yes</td>
<td>13 h</td>
<td>Respiratory failure</td>
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<tr>
<td>7 700</td>
<td>17</td>
<td>76</td>
<td>–</td>
<td>No</td>
<td>Yes</td>
<td>7 h</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td>8 875</td>
<td>19</td>
<td>40</td>
<td>7.29</td>
<td>Yes</td>
<td>No</td>
<td>5 months</td>
<td>Chronic lung disease</td>
</tr>
<tr>
<td>9 1803</td>
<td>19</td>
<td>71</td>
<td>–</td>
<td>Yes</td>
<td>Yes</td>
<td>9 months</td>
<td>Chronic lung disease</td>
</tr>
<tr>
<td>10 2722</td>
<td>17</td>
<td>111</td>
<td>7.31</td>
<td>Yes</td>
<td>Yes</td>
<td>18 h</td>
<td>Respiratory failure</td>
</tr>
</tbody>
</table>

Everest et al ADCF&N 2007

Preterm infants with extreme PPROM
RHH Hobart 2004-2012

Membrane rupture <25 weeks
Minimal latent period 14 days
Gestation at birth ≥ 24 weeks

If needing intubation:
• Conventionally ventilated (Babylog or Neopuff)
• Surfactant given
• Early transition to HFOV (Sensormedics) if:
  • Remaining in FiO₂ > 0.4
  • Respiratory acidosis, pH < 7.25
• iNO only used for refractory hypoxia

Aiyappan et al PSANZ abstract, JCPH 2010
Preterm infants with extreme PPROM
RHH Hobart 2004-2012

Aiyappan et al PSANZ abstract, JCPH 2010

20 infants born alive
4 infants on CPAP from the outset (2 intubated beyond 1st week)
16 infants intubated on day 1
9 stabilised on CMV
7 infants had refractory hypoxic respiratory failure on CMV and had early transition to HFOV (mean age 2 hrs)

Extreme PPROM RHH Hobart
Infants with refractory hypoxia on CMV (n=7)

\[ \text{FiO}_2 \]

\[ \text{pCO}_2 \]

\[ \text{pH} \]

\[ \text{PAW} \]
HFOV in pulmonary hypoplasia

- Pulmonary hypoplasia
  - Small but often biochemically mature lung
  - Structurally immaturity, high susceptibility to barotrauma
  - High pulmonary vascular resistance

**APPROACH:**
- Early transition to HFOV if failing on CMV
- Low pressure strategy
  - Initial $P_{AW}$ 10-15 cm H$_2$O ($\leq P_{AW}$ on CMV)
  - Frequency 10-12 Hz
  - Wait for an effect
  - Gentle stepwise recruitment only if oxygenation remains poor and lung parenchyma is opacified
- Initially allow minimal or no spontaneous respiration
  - Sedation and muscle relaxation
- Treat co-existing PPHN with iNO if failing to oxygenate after time on HFOV
Pulmonary hypoplasia with overdistension

Extreme PPROM RHH Hobart
Infants with refractory hypoxia on CMV (n=7)
Extreme PPROM RHH Hobart
Infants with refractory hypoxia on CMV (n=7)

Preterm infants with extreme PPROM
RHH Hobart 2004-2012

20 infants born alive (24-31 weeks)
Early HFOV in 7/20 (35%)
None died on day 1
All survived to discharge
One death post-discharge (PVL)

Aiyappan et al PSANZ abstract, JCPH 2010
Preterm infants with extreme PPROM
Royal North Shore 2000-2008
Membrane rupture ≤24 weeks
Minimal latent period 14 days

Shah & Kluckow JCPH 2011

Bay 3 L CDH
HFOV in CDH

“...for many, the management of the newborn with CDH is more emotional than scientific.”

Glick, Irish & Holm Clin Perinatol 1996

HFOV in CDH

“...unlike the other neonatal pulmonary diseases, CDH does not represent a recruitable lung and attempts to use a high mean airway pressure are likely to cause pulmonary damage”.

Bohn AJRCCM 2002
The CDH lung

Kotecha et al Eur Respir J 2012

The CDH lung vasculature

Levin J Pediatr 1978
HFOV in CDH
The evidence

Clinical Commentary

Congenital Diaphragmatic Hernia

Am J Respir Crit Care Med Vol 166, pp 911–915, 2002

Consensus Statement

Neonatology

Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe: The CDH EURO Consortium Consensus

ERS TASK FORCE REPORT

Congenital diaphragmatic hernia

HFOV in CDH

Retrospective study of 111 cases of congenital diaphragmatic hernia treated with early high-frequency oscillatory ventilation and presurgical stabilization

Lucia Migliazza*, Cristina Bellana, Daniele Alberti, Antonietta Auricemma, Giampiero Burgio, Giuseppe Locatelli e Angelo Colombo


Protocolized approach to the management of congenital diaphragmatic hernia: benefits of reducing variability in care


HFOV in CDH

<table>
<thead>
<tr>
<th>TABLE 1. OUTLINE OF PRINCIPLES OF MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resuscitation</td>
</tr>
<tr>
<td>ET tube placement with minimal bag mask/ventilation</td>
</tr>
<tr>
<td>Vascular access</td>
</tr>
<tr>
<td>Gut decompression by nasogastric tube</td>
</tr>
<tr>
<td>Ventilation objectives: preductal SaO2 &gt; 85% and pH &gt; 7.3 with PIP &lt; 25 cm H2O</td>
</tr>
<tr>
<td>Cardiopulmonary management</td>
</tr>
<tr>
<td>Ventilation</td>
</tr>
<tr>
<td>Conventional ventilation</td>
</tr>
<tr>
<td>Objective: preductal SaO2 &gt; 85% pH &gt; 7.3</td>
</tr>
<tr>
<td>PIP &lt; 25 cm H2O</td>
</tr>
<tr>
<td>HFOV</td>
</tr>
<tr>
<td>Objective: preductal SaO2 &gt; 85%</td>
</tr>
<tr>
<td>MAP &lt; 16 cm H2O</td>
</tr>
<tr>
<td>Pulmonary vascular management</td>
</tr>
<tr>
<td>Cardiac echo</td>
</tr>
<tr>
<td>Exclude CHD</td>
</tr>
<tr>
<td>Assess RV function</td>
</tr>
<tr>
<td>Estimate PA pressure</td>
</tr>
<tr>
<td>Identify the ductus and assess shunting</td>
</tr>
<tr>
<td>Trial of inhaled nitric oxide for patients with increased RV pressure</td>
</tr>
</tbody>
</table>

Bohn AJRCCM 2002
## Ventilation in CDH

### Initial Management at Delivery

**Immediate intubation**
- Immediate ventilation goals: pre-ductal O2 sat >95%, PIP goal <24

- If PIP >26 and/or MAP >12 to achieve PaCO₂ <65mmHg, HFV will be used
- If PIP >26 with conventional ventilator to maintain ideal parameters, intial HFV will be with jet ventilation

### Management practices

<table>
<thead>
<tr>
<th>Study</th>
<th>Routine CS delivery?</th>
<th>Intubation at delivery?</th>
<th>NG tube at delivery?</th>
<th>Pre-ductal SpO₂</th>
<th>Post-ductal SpO₂</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bohn 2001</td>
<td>NS</td>
<td>Yes</td>
<td>Yes</td>
<td>&gt;85%</td>
<td>70%</td>
<td>7.3</td>
</tr>
<tr>
<td>ERS Taskforce 2012</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>&gt;85%</td>
<td>NS</td>
<td>7.2</td>
</tr>
<tr>
<td>Euro Consortium 2010</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>&gt;85%</td>
<td>70%</td>
<td>7.2</td>
</tr>
<tr>
<td>Tracy 2010</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>&gt;85%</td>
<td>70%</td>
<td>7.25</td>
</tr>
<tr>
<td>Migliazza 2007</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>&gt;85%</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>RWH-RCH</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>&gt;85% (70%)</td>
<td></td>
<td>7.2</td>
</tr>
</tbody>
</table>

**NA:** not applicable, **NS:** not stated

---

## HFOV in CDH

### Management practices

- **SAFE ZONE**
  - CV, PIP <26
  - HFOV or HFJV: MAP <16
  - Dopamine infusion < 20 mcg/kg/min
  - Epinephrine infusion < 0.1 mcg/kg/min to maintain MAP > 50 mm Hg

- **CAUTION ZONE**
  - CV, PIP 26-30
  - HFOV or HFJV: MAP 16-22
  - Dopamine infusion 20 mcg/kg/min with Epinephrine infusion 0.1 – 0.3 mcg/kg/min to maintain MAP > 50 mm Hg
  - Consideration of INO

- **HAZARD ZONE**
  - CV, PIP >30
  - HFOV or HFJV: MAP >22
  - Dopamine infusion 20 mcg/kg/min with Epinephrine infusion > 0.3 mcg/kg/min to maintain MAP > 50 mm Hg

Tracy et al. *Pediatr Surg* 2010
HFOV in CDH
Management practices

<table>
<thead>
<tr>
<th>CMV settings</th>
<th>HFOV settings</th>
<th>Muscle relaxants</th>
<th>iNO use</th>
<th>ECMO use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max PIP</td>
<td>PEEP range</td>
<td>Max Paw</td>
<td>deltP</td>
<td>I:E</td>
</tr>
<tr>
<td>Bohn 2001</td>
<td>25 cm H2O</td>
<td>NS</td>
<td>15</td>
<td>35-45</td>
</tr>
<tr>
<td>ERS Taskforce 2012</td>
<td>25 cm H2O</td>
<td>&lt;5 cm H2O</td>
<td>17</td>
<td>NS</td>
</tr>
<tr>
<td>Euro Consortium 2010</td>
<td>28 cm H2O</td>
<td>2-5 cm H2O</td>
<td>17</td>
<td>30-50</td>
</tr>
<tr>
<td>Tracy 2010</td>
<td>26 cm H2O</td>
<td>NS</td>
<td>22*</td>
<td>NS</td>
</tr>
<tr>
<td>Miglazza 2007</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>30-40</td>
</tr>
<tr>
<td>RWH-RCH</td>
<td>25 cm H2O</td>
<td>3-5 cm H2O</td>
<td>15</td>
<td>30-50</td>
</tr>
</tbody>
</table>

NA: not applicable, NS: not stated;
*Sensormedics oscillator; †1:2 with Sensormedics, other oscillators and HFJV also used

HFOV in CDH
The VICI trial

- HFOV (n=80) compared with CMV (n=91)
- Prenatally diagnosed CDH
- Mx according to Euro Consortium protocol
- Of 80 managed on HFOV initially, 48 crossed over to CMV or ECMO
- On intention-to-treat analysis:
  - No difference in survival free of oxygen at 28 days
  - Less “treatment failures” in CMV group
  - Shorter duration of ventilation in CMV group

Snoek et al  EAPS abstract 2014
L CDH immediately post-op
L CDH day 1 post-op
L CDH day 2 post-op
L CDH day 3 post-op
L CDH day 4 post-op
L CDH showing early overdistention and cystic change
L CDH – gross overinflation of the L lung

HFOV in CDH

Therapies for CDH at RCH Melbourne

<table>
<thead>
<tr>
<th>TIME EPOCH</th>
<th>ECMO</th>
<th>HFO/JV</th>
<th>iNO</th>
<th>PGE1</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 1981-1991</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2 1992-1995</td>
<td>9%</td>
<td>13%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>3 1996-1999</td>
<td>11%</td>
<td>52%</td>
<td>48%</td>
<td>0%</td>
</tr>
<tr>
<td>4 2000-May 2003</td>
<td>7%</td>
<td>46%</td>
<td>36%</td>
<td>0%</td>
</tr>
<tr>
<td>5 May 2003-end 2005</td>
<td>3%</td>
<td>73%</td>
<td>72%</td>
<td>68%</td>
</tr>
<tr>
<td>6 2006-2014</td>
<td>5%</td>
<td>83%</td>
<td>60%</td>
<td>70%</td>
</tr>
</tbody>
</table>

RCH CDH Survival 2006-2014

- N=124 liveborn infants
- Antenatal diagnosis 65%
- Left 80% Rt 20%

- Survival (all) 76%
- Survival (excluding major anomalies) 78%
29 weeks, day 11, on nasal CPAP
resp acidosis and increasing FiO₂

Bay 4 Cystic lung disease / PIE

Jet ventilation experience at RCH

28/40, day 25, pre- jet ventilation, FiO₂ 1.0
16 hours after HFJV, FiO₂ 0.3
Preterm infants with cystic PIE
RHH Hobart 2004-2011

<table>
<thead>
<tr>
<th></th>
<th>Bilateral (n = 14)</th>
<th>Unilateral (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation, weeks</td>
<td>25 (25–25.8)</td>
<td>27 (25–27)</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>775 (715–850)</td>
<td>1,150 (760–1,258)</td>
</tr>
<tr>
<td>Day of life PIE first evident</td>
<td>7.5 (2–17)</td>
<td>6 (3–22)</td>
</tr>
<tr>
<td>Age at transition to low frequency HFOV, days</td>
<td>20 (7.8–39)</td>
<td>12 (12–27)</td>
</tr>
<tr>
<td>Pre-transition ventilation mode</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFOV</td>
<td>14 (88%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>CMV</td>
<td>1 (6%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>CPAP</td>
<td>1 (6%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Pre-transition FiO2</td>
<td>0.6 (0.5–0.7)</td>
<td>0.53 (0.4–0.8)</td>
</tr>
<tr>
<td>Pre-transition PCO2, mm Hg</td>
<td>57 (48–63.5)</td>
<td>62 (57–78.4)</td>
</tr>
</tbody>
</table>

Median (IQR) or n (%)  Squires et al Neonatology 2013

HFOV in cystic lung disease / PIE

**PLAN:**
- Use the oscillator in a manner that allows the cysts to empty more effectively with each oscillatory cycle
- Ultimate aim is to encourage gas to resorb from the interstitium, and airspaces to then re-expand

**APPROACH:**
- Use an oscillator with active expiration
HFOV in cystic lung disease / PIE

**PLAN:**
- Use the oscillator in a manner that allows the cysts to empty more effectively with each oscillatory cycle
- Ultimate aim is to encourage gas to resorb from the interstitium, and airspaces to then re-expand

**APPROACH:**
- Use an oscillator with active expiration
- Low pressure strategy
  - $P_{aw}$ 10-14 cm H$_2$O
  - the lowest possible $P_{aw}$ whilst maintaining oxygenation
  - no recruitment manoeuvres
  - accept high $FiO_2$
- Frequency 5 Hz
  - = low frequency high frequency ventilation
  - beware hypocarbia
- Initially allow no spontaneous respiration
  - sedation and muscle relaxation
  - allow spontaneous breathing once PIE improved (usually only 2-3 days)
- Positioning
  - good lung uppermost
Unilateral cystic lung disease

Before low pressure, low frequency HFOV

24 hrs
$P_{AW}$ 11, freq 5 Hz
$FiO_2$ 0.21

72 hrs
$P_{AW}$ 7, freq 5 Hz
$FiO_2$ 0.35

Unilateral cystic lung disease

84 hrs
$P_{AW}$ 7, freq 5 Hz
$FiO_2$ 0.30

104 hrs
$P_{AW}$ 7, freq 12
$FiO_2$ 0.21
Bilateral cystic lung disease

24 weeks, day 15 transferred to HFOV

day 18, $P_{AW}$ 12, freq 5 Hz
$FiO_2$ 1.0

day 21, $P_{AW}$ 10, freq 5 Hz
$FiO_2$ 0.5

Squires et al. *Neonatology* 2013
Preterm infants with cystic PIE
RHH Hobart 2004-2011

<table>
<thead>
<tr>
<th></th>
<th>Bilateral (n = 14)</th>
<th>Unilateral (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival</td>
<td>10 (71%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>BPD (in survivors)</td>
<td>9 (90%)</td>
<td>4 (80%)</td>
</tr>
</tbody>
</table>

Squires et al Neonatology 2013

HFOV IN THE NON-RECRUITABLE LUNG

Summary

- Use (or avoidance) of recruitment manoeuvres should take into account:
  - degree of parenchymal disease
  - susceptibility of the lung to barotrauma
  - state of the pulmonary vasculature
- A “low pressure” strategy with time dependent recruitment can be very effective if aggressive recruitment is contraindicated
- Low frequency HFOV (freq = 5) can help to decompress overdistended lung regions