Optimizing Mechanical Ventilation: The Art and Science

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Objectives

• Review the components of mechanical ventilation
• Discuss options for choosing initial ventilator settings based on individual pathophysiology
• Consider ways to avoid oxygen toxicity
• Outline strategies for weaning
Neonatal Ventilation ca. 1975

One Size Fits All
The Baby Bird

- Flow 8-10 LPM
- PIP 20 cm H₂O
- PEEP 4 cm H₂O
- Tᵢ 0.4 sec
It Didn’t Matter…

Preterm Baby RDS  Term Baby MAS
It Didn’t Matter...

Preterm Baby RDS

Term Baby MAS
Optimizing Mechanical Ventilation: Choosing the Initial Settings
A Patient

- 25 weeks, 720 grams
- 17 y/o G₁P₀
- C/S for severe pre-eclampsia, treated with MgSO₄
- One dose of betamethasone to mom
- Apgar scores 2 (HR 136) and 5 (HR 140, color pink with bagging, no tone, no respiratory effort, minimal grimace)
Initial Evaluation

- ABG: 7.21/55/47
- Hgb/Hct: 14.0/43%
- Cord Mg\(^{++}\): 5.5
- BP: 36/20 (25)
Define the Pathophysiology

- Lung volumes?
- Compliance?
- Resistance?
- Time constant?
- Respiratory drive?
- Oxygenation?
- Ventilation?
Initial Ventilatory Options

• CPAP
• Conventional (tidal) ventilation
• High-Frequency ventilation
  - HFJV
  - HFOV
Target Variables

• Pressure
  ➢ Pressure Limited
  ➢ Pressure Control

• Volume
Ventilator-Induced Lung Injury

**Atelectotrauma:**
Repetitive alveolar opening and closing of under-recruited alveoli

**Volutrauma:**
Over-distension of normally aerated alveoli from excessive volume delivery

- Demonstrated severe acute lung injury occurred in small animals using large $V_T$
- When the chest cavity was bound and the lungs exposed to high pressures, the acute lung injury markers were much lower than the injury that ensued once the binding was removed
- Excessive $V_T$ -and not high pressure- is primarily responsible for lung injury
A large $V_T$ injected into a critter with a strapped chest doesn’t hurt its lungs:

Even if PIP is very high!
If one pushes in that same $V_T$ without the strap, it causes the lungs to burst:

Even if PIP is not very high!
Volume vs. Pressure

**Volume**

“Back end-loaded”

**Pressure**

“Front end-loaded”

Flow

Pressure
Pressure vs. Volume
(Control variables)
## Mortality

### 1.1.1 Incidence of death

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>VTV Events</th>
<th>Total</th>
<th>PLV Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>D’Angio CT2005</td>
<td>13</td>
<td>104</td>
<td>13</td>
<td>107</td>
<td>21.1%</td>
<td>1.03 [0.50, 2.11]</td>
<td></td>
</tr>
<tr>
<td>Duman N2012</td>
<td>3</td>
<td>23</td>
<td>7</td>
<td>22</td>
<td>11.8%</td>
<td>0.41 [0.12, 1.39]</td>
<td></td>
</tr>
<tr>
<td>Guven S2013</td>
<td>3</td>
<td>42</td>
<td>5</td>
<td>30</td>
<td>9.6%</td>
<td>0.43 [0.11, 1.66]</td>
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</tr>
<tr>
<td>Keszler M2004</td>
<td>1</td>
<td>9</td>
<td>1</td>
<td>9</td>
<td>1.6%</td>
<td>1.00 [0.07, 13.64]</td>
<td></td>
</tr>
<tr>
<td>Lista G2004</td>
<td>5</td>
<td>30</td>
<td>6</td>
<td>23</td>
<td>11.2%</td>
<td>0.64 [0.22, 1.84]</td>
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<tr>
<td>Liu CQ2011</td>
<td>2</td>
<td>31</td>
<td>3</td>
<td>30</td>
<td>5.0%</td>
<td>0.65 [0.12, 3.59]</td>
<td></td>
</tr>
<tr>
<td>Nafday SM2005</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>18</td>
<td>1.5%</td>
<td>2.25 [0.22, 22.53]</td>
<td></td>
</tr>
<tr>
<td>Piotrowski A2007</td>
<td>7</td>
<td>30</td>
<td>4</td>
<td>26</td>
<td>7.1%</td>
<td>1.52 [0.50, 4.60]</td>
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<tr>
<td>Piotrowski A1997</td>
<td>4</td>
<td>27</td>
<td>8</td>
<td>31</td>
<td>12.3%</td>
<td>0.57 [0.19, 1.70]</td>
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</tr>
<tr>
<td>Singh J2006</td>
<td>5</td>
<td>57</td>
<td>10</td>
<td>52</td>
<td>17.2%</td>
<td>0.46 [0.17, 1.25]</td>
<td></td>
</tr>
<tr>
<td>Sinha SK1997</td>
<td>1</td>
<td>25</td>
<td>1</td>
<td>25</td>
<td>1.6%</td>
<td>1.00 [0.07, 15.12]</td>
<td></td>
</tr>
<tr>
<td>**Subtotal (95% CI)</td>
<td>394</td>
<td>373</td>
<td><strong>100.0%</strong></td>
<td><strong>46</strong></td>
<td>59</td>
<td><strong>0.73 [0.51, 1.05]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 46, 59

Heterogeneity: $\chi^2 = 6.13$, df = 10 ($P = 0.80$); $I^2 = 0$

Test for overall effect: $Z = 1.71$ ($P = 0.09$)
## Incidence of BPD

### 1.2.1 Incidence of BPD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>VTV Events</th>
<th>Total</th>
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<td>27</td>
<td>93</td>
<td>32</td>
<td>92</td>
<td>35.0%</td>
<td>0.83 [0.55, 1.27]</td>
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<tr>
<td>Duman N2012</td>
<td>3</td>
<td>23</td>
<td>7</td>
<td>22</td>
<td>7.8%</td>
<td>0.41 [0.12, 1.39]</td>
<td></td>
</tr>
<tr>
<td>Guven S2013</td>
<td>2</td>
<td>42</td>
<td>9</td>
<td>30</td>
<td>11.4%</td>
<td>0.16 [0.04, 0.68]</td>
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</tr>
<tr>
<td>Keszler M2004</td>
<td>2</td>
<td>9</td>
<td>5</td>
<td>9</td>
<td>5.4%</td>
<td>0.40 [0.10, 1.55]</td>
<td></td>
</tr>
<tr>
<td>Lista G2004</td>
<td>3</td>
<td>30</td>
<td>4</td>
<td>23</td>
<td>4.9%</td>
<td>0.57 [0.14, 2.32]</td>
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</tr>
<tr>
<td>Nafday SM2005</td>
<td>2</td>
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<td>4</td>
<td>18</td>
<td>4.1%</td>
<td>0.56 [0.12, 2.67]</td>
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<tr>
<td>Singh J2006</td>
<td>16</td>
<td>57</td>
<td>17</td>
<td>52</td>
<td>19.3%</td>
<td>0.86 [0.49, 1.52]</td>
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<tr>
<td>Sinha SK1997</td>
<td>1</td>
<td>25</td>
<td>6</td>
<td>25</td>
<td>6.5%</td>
<td>0.17 [0.02, 1.29]</td>
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<tr>
<td>Zhou XJ2007</td>
<td>2</td>
<td>15</td>
<td>5</td>
<td>15</td>
<td>5.4%</td>
<td>0.40 [0.09, 1.75]</td>
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</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>310</strong></td>
<td><strong>286</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td><strong>0.61 [0.46, 0.82]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 58 | 89

Heterogeneity: Chi² = 9.37, df = 8 (P = 0.31); I² = 15%

Test for overall effect: Z = 3.36 (P = 0.0008)

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VTV reduced the incidence of BPD, duration of mechanical ventilation, failure of primarily assigned ventilatory mode, grades 3/4 IVH, PVL and air leaks compared to PLV modes.  

[Peng, IBID]
Volume Targeting

- Adjust pressure or volume to provide 4-7 mL/kg
- Avoid both hyperinflation and underinflation
- A happy baby will breathe at 40-60 bpm
Mode

- IMV
- SIMV
- Assist/Control
Cycling

- Time
- Flow
Inspiratory Time

- Time Constant
- I:E ratio
- Gas trapping
• One size does not fit all
• Optimize inflation
• Find best compliance
Flow

- Avoid rheotrauma
- If too high
  - Turbulence
  - Inadvertent PEEP
- If too low
  - Flow starvation
  - Inability to reach PIP or desired Vt
Rate

- Encourage spontaneous breathing
- Provide adequate safety net
- Follow minute ventilation, if possible
• Set at lowest level that avoids autocycling
Oxygen Therapy: Can We Get It Right?
Introduction

Oxygen

- An integral part of all respiratory support
- One of the most commonly used drugs in the neonatal intensive care unit
Introduction

Goal of Oxygen Therapy:

- To achieve adequate delivery of oxygen to the tissues without creating oxygen toxicity
The recent trials of oxygen therapy suggest that lower SpO2 can reduce severe retinopathy of prematurity (ROP), but is associated with a higher mortality.

• Babies often display wide fluctuations in SpO2

• How can we better control both oxygen delivery and limit these fluctuations?
Closed-Loop Control of Oxygenation
Most preterm infants exhibit spontaneous fluctuations in $\text{SpO}_2$.

Preterm infants often require supplemental oxygen, increasing risk of:
- Retinopathy of prematurity
- Lung injury
- Oxidative stress injury
- Necrotizing enterocolitis
Background

- Delayed responses to these fluctuations result in hyperoxemic and hypoxemic episodes, as well as:
  - Increased risk of impaired oxygen delivery
  - Increased risk of ROP and chronic lung disease
Only about 50% of the time, is SpO₂ within the desired range.

- Laptook et al (J Perinatol 2006)
  - N=74, 1 center, 19 months
  - 27% below, 58% within, 15% above

- Hagadorn et al (Pediatrics 2006)
  - N=84, 14 centers (3 countries), 8 months
  - 16% below, 48% within, 36% above
“The computer allows you to make mistakes faster than any other invention, with the possible exception of handguns and alcohol.”

- Mitch Ratcliffe
Closed-Loop

Desired Value ➔ +/- ➔ Controller Algorithm ➔ Controller ➔ New Value ➔ Desired Value

Controller Algorithm
Closed-Loop

Proportion – Integral - Derivative
Closed-Loop Control

- Goal
  - Minimize time out of target SpO₂ range, especially high SpO₂
  - Reduce modulation of SpO₂
Algorithm Goals

- **Normoxemia**
  - Minimize change in $SPO_2$
  - Gradually wean $FIO_2$
- **Hypoxemia**
  - Rapidly increase $FIO_2$ to bring $SPO_2$ in bounds
    - Reduce $FIO_2$ as $SpO_2$ approaches target.
- **Hyperoxemia**
  - Minimize the further increase in $SPO_2$
  - Gradually wean $FIO_2$
CLiO$_2$ Pilot Trial Summary

- In ventilated infants with frequent episodes of hypoxemia, automated regulation of FiO$_2$ in comparison to routine care:
  - Increased time within intended SpO$_2$ range
  - Reduced severe hyper- and hypoxemia
  - Reduced the fraction of inspired O$_2$
  - Reduced manual interventions

Automated Adjustment of Inspired Oxygen in Mechanically Ventilated Preterm Infants: A Multicenter Crossover Trial


1 University of Miami
2 Ohio State University
3 University of Southern California
4 University of Michigan
5 California State University
In ventilated preterm infants with frequent fluctuations in oxygenation, automated FiO$_2$ adjustment is more effective than standard care in maintaining SpO$_2$ within the intended range under routine clinical conditions.
Hypotheses

- Automated FiO$_2$ adjustment reduces severe hyper- and hypoxemia, supplemental O$_2$ and the number of manual FiO$_2$ adjustments
To evaluate the efficacy and safety of automated FiO$_2$ adjustment in maintaining SpO$_2$ within the intended range in preterm infants with frequent spontaneous episodes of hypoxemia in the standard clinical setting in a multicenter crossover trial.
Study Approval

- Approved by the each institution’s IRB
- Conducted under approval for use of the “Automated FiO₂ Adjustment Function” of the Avea infant ventilator as an investigational device by the US FDA (G060031/S009)
- Written informed parental consent
Eligibility

- Preterm infants on supplemental O₂ and mechanical ventilation
- Frequent spontaneous episodes of hypoxemia (SpO₂<80%, ≥ 4 episodes per 8 hrs., during previous 24 hrs.)
- Hemodynamically stable
- Absence of major congenital anomalies
- Absence of seizure activity
- Absence of ongoing sepsis or meningitis
Study Protocol

- Two consecutive periods:
  - 24 hrs. with FiO₂ adjusted routinely by clinical staff (Standard)
  - 24 hrs. of automated FiO₂ adjustment (Automated)

- Sequence assigned by random blocks per center

- The intended SpO₂ range for both periods was 87 - 93%
Automated FiO₂ function:

- FiO₂ is ↑ or ↓ step-wise if SpO₂ is < or > the intended range
- Magnitude and frequency of FiO₂ adjustments are determined by:
  - difference between SpO₂ and intended range
  - time outside range
  - trend in SpO₂
  - basal FiO₂
- Basal FiO₂ is adjusted gradually to keep SpO₂ within range
Study Population

Birth weight: 671 ± 156 g
Gestational age: 25 ± 2 w
Postnatal age: 26 ± 15 d
Rate: 27 ± 10 bpm
PIP: 22 ± 6 cm H$_2$O
PEEP: 6 ± 1 cm H$_2$O
PSV: 8 ± 2 cm H$_2$O
FiO$_2$: 37 ± 11 %
Hourly Median $\text{SpO}_2$ and $\text{FiO}_2$

**:p<0.05 Two way RM ANOVA**

Intended range

- **Standard**
- **Automated**
Time Within or Above Intended Range

SpO₂ 87-93%  SpO₂ > 93%  SpO₂ > 98%
(@ FiO₂ > 21%)  (@ FiO₂ > 21%)

*: p < 0.001 Paired t-test
**: p = 0.003 Wilcoxon Test
(median, quartiles)
Time Below Intended Range

- SpO₂ < 87%
- SpO₂ < 75%

**:p<0.001 Paired t-test (mean±SD)**

Bar chart showing percentage of time below SpO₂ values with standard and automated methods.
Prolonged Episodes Below Intended Range

**Prolonged Episodes Below Intended Range**

- **SpO₂ < 85%** (＞120 sec)
- **SpO₂ < 75%** (＞60 sec)

**p<0.001** Paired t-test (mean ± SD)

**p=0.001** Wilcoxon Signed Rank Test (median and 25th – 75th percentile)

Data from [Standard] and [Automated] systems.
24 Hr Median FiO\textsubscript{2} and Manual Adjustments

*: p<0.001 Paired t-test (mean±SD)
These data from a group of preterm infants with frequent fluctuations in SpO₂, obtained under standard clinical conditions, showed that:

**Automated FiO₂ adjustment**

- improved maintenance of SpO₂ within the intended range
- reduced hyperoxemia, supplemental O₂, and staff workload

Conclusions
The increased number of mild episodes with SpO$_2$ below the intended range is likely related to FiO$_2$ weaning and avoidance of hyperoxemia.
Limitations

- Automated FiO₂ should not be a substitute for more appropriate observations or interventions.
- Automated FiO₂ may give an excessive sense of confidence and lead to reduced attentiveness.
Limitations

- Automated FiO₂ is dependent on pulse oximetry accuracy
- Observed differences in this study may be relative to the effectiveness of standard care
- Physiologic consequences of different targeted SpO₂ ranges should be taken in consideration
WEANING INFANTS FROM MECHANICAL VENTILATION
Weaning

The process of transferring the work of breathing from the ventilator to the baby.
Weaning

• Weaning- or at least the consideration to wean- should begin as soon as a baby is intubated.
Weaning and Extubation

- Still largely determined by personal preferences
- Tends to be experiential or anecdotal
- Very little clinical data
Weaning is a Dynamic Process

• Changing disease and/or patient status
• Interaction between heart and lungs (e.g., PDA)
• Caloric intake vs. expenditure
• Relationship between central control of breathing and respiratory muscles
Physiologic Essentials for Extubation

- Reliable respiratory drive
- Neuromuscular competence
- Reduction in respiratory system load
Impediments to Successful Weaning

- Infection
- Neurologic dysfunction
- Neuromuscular incompetence
- Inadequate caloric intake
- Excessive fat/CHO intake
Impediments to Successful Weaning

- Electrolyte imbalance
- Metabolic alkalosis
- Congestive heart failure
- Anemia
- Pharmacologic agents
“The biggest reason for failure to wean is failure to wean.”

-Donn