Mechanism of Action and Physiology of HiFlo

John Fraser
Prince Charles Hospital
University of Queensland
Seoul
2015
Declarations

- FP - grant support and travel
- Draeger - EIT
- Macquet - NAVA
- CRE
A Palatial Analogy

Clinical Use

Physiological Outcomes

Mechanism
K.I.S.S. Principles

HiFlo

Flow
Humidification
• **Aim**

- To determine the effects of heated humidification therapy on mucociliary clearance in patients with bronchiectasis

- • N=14

- • Radio aerosol technique used to measure mucociliary clearance before and after 7 days of domiciliary humidification, delivered at flow rates 20-25 L/min for 3 hours daily
Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis

A Hasani¹, TH Chapman², D McCool³, RE Smith¹, JP Dilworth² and JE Agnew¹

- Area under the curve decreased $p<0.0007$

- Mucociliary clearance was enhanced post treatment
Relevance to ICU patients

31 Degrees Dry

37 Degrees moist
Flow Rate – What does this DO and where?
Breathing profile standard nasal cannula
4L/min with entrainment of air: Peak inspiratory demand not met

Breathing profile HiFlo
35L/min with zero entrainment Room Air Peak inspiratory demand met
Modelling flow in Upper Airway
Airway Anatomy
Airway Modelling
Natural Breathing - Expiration
Natural Breathing - Inspiration

Velocity [m/s]
HiFlo 40 L/min - Expiration
HiFlo 40 L/min - Inspiration
Nasal high flow clears $^{81m}$Kr-gas from upper airways in healthy volunteers

Results: $^{81m}$Kr-gas in subjects & CO$_2$-gas clearance in a model

What effect on Tidal Volumes
Mechanisms of nasal high flow on ventilation during wakefulness and sleep

Toby Mündel,1 Sheng Feng,2 Stanislav Tatkov,2 and Hartmut Schneider3
1School of Sport and Exercise, Massey University, Palmerston North, New Zealand; 2Fisher & Paykel Healthcare, Auckland, New Zealand; 3Division of Pulmonary and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland
Mechanisms of nasal high flow on ventilation during wakefulness and sleep


- Healthy individuals
Differences between CPAP and HiFlo

- **NHF Reduces the Proportion of Dead-Space Ventilation during Wakefulness and Sleep**
But what happens at the sick alveolus?
EIT operation

208 measures/ frame
(16 x 13 voltages)
EIT – Real Time analysis
Transition from 6L Hudson Mask to HiFlo 30 L
Correlation between Lung Impedance & Lung Volume

The relationship between impedance change and lung volume is highly linear

End Expiratory Lung Impedance ≈ End Expiratory Lung Volume

\[ r = 0.95 \]

\[ r = 0.97 \]


Complications post Cardiac surgery

- Patients are older with more co-morbidities
- Atelectasis and lobar collapse occurs in most post cardiac surgical patients due to:
  - Decrease in FRC by ~20% during anaesthesia
  - Median sternotomy reduces PEFR by 65%
  - Pleural effusions secondary to IMA harvest
  - Diaphragm dysfunction
  - Hypoventilation
  - Sternal pain
  - Narcotic use
Study Design and Aims

Design
- Prospective observational study

Aims
- To establish if Nasal High Flow increases EELV when compared with mask O2
- To correlate changes in EELV with changes in oropharyngeal airway pressure (AP)
- To investigate if Nasal High Flow:
  - improves gas exchange,
  - increases Tidal Volumes (TV)
  - decreases Respiratory Rate (RR)
Airway Pressure reading

![Graph showing airway pressure over time with red and blue lines indicating HIGH and LOW, respectively. The graph includes markers for 4.4 cmH₂O and 0 cmH₂O.]
Physiological Effect of HFNC in infants with Bronchiolitis
Change in End-Expiratory Level

Pham T et al. Ped Pulmonol 2014
HiFlo effect at the lung - not just upper airway

30L Flow

50 L Flow
End Expiratory Lung Volume

Equates to a 25.6% increase in EELV on high flow when compared to low flow oxygen (CI 24.3, 26.9)

p < 0.001
PaO$_2$/FiO$_2$ Ratio

LOW

HIGH

Mean increase of 30.6mmHg (CI 17.9, 43.3)

p < 0.001
Respiratory Rate

LOW          HIGH
Mean decrease of 3.4 breaths per minute (CI 2.0, 4.7)

p < 0.001
Tidal Variation
(correlates with Tidal Volume)

Equates to 10% increase in tidal variation
(CI 6.1 - 18.3)

p < 0.001
Can Modelling of Deadspace Reduction Explain Result?

**Normal Lung**

- Anatomic Deadspace (150ml)
- Fresh gas reaching lung (350ml)
- Tidal Volume (500ml)

AV = (500ml – 150ml) x 12 bpm = 4.2 L/min

MV = 500ml x 12 bpm = 6 L/min

**Sick Lung**

- Anatomic Deadspace (150ml)
- Fresh gas reaching lung (200ml)
- Tidal Volume (500ml)

The volume range is 0 to 500 ml.

AV = 4.2L/min / (500ml – 300ml) = 21bpm

MV = 500ml x 21bpm = 10.5L/min

**Sick Lung with Hiflo**

- Anatomic Deadspace (100ml)
- Fresh gas reaching lung (250ml)
- Tidal Volume (500ml)

AV = 4.2L/min / (500ml – 250ml) = 16.8bpm

MV = 500ml x 16.8bpm = 8.4L/min
Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients

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2 Institute of Health and Biomedical Innovation, School of Public Health, Queensland University of Technology, 60 Musk Avenue, Kelvin Grove, QLD 4059, Australia

Table 2: Outcome variables. Low-flow oxygen compared with HFNCs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low-flow oxygen [mean (sd)]</th>
<th>HFNC [mean (sd)]</th>
<th>Mean difference [mean (sd)]</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-expiratory lung impedance (units)</td>
<td>419 (212.5)</td>
<td>1936 (212.9)</td>
<td>1517 (46.6)</td>
<td>1425, 1608</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean airway pressure (cm H2O)</td>
<td>−0.3 (0.9)</td>
<td>2.7 (1.2)</td>
<td>3.0 (1.3)</td>
<td>2.4, 3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory rate (bpm)</td>
<td>20.9 (4.4)</td>
<td>17.5 (4.6)</td>
<td>−3.4 (2.8)</td>
<td>−2.0, −4.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Borg score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–10</td>
<td>2.7 (2.6)</td>
<td>1.9 (2.3)</td>
<td>−0.8 (1.2)</td>
<td>−0.1, −1.4</td>
<td>0.023</td>
</tr>
<tr>
<td>Tidal variation (units)</td>
<td>1512 (195.0)</td>
<td>1671 (195.1)</td>
<td>159 (21.6)</td>
<td>117, 201</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PaO2/FiO2 ratio (mm Hg)</td>
<td>160 (53.7)</td>
<td>190.6 (57.9)</td>
<td>30.6 (25.9)</td>
<td>17.9, 43.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
EELV by Body Mass Index

p < 0.001

13.3%

24.4%
Using this mechanism, could we prevent deterioration?

- Prevent ICU admission
- Earlier intervention prior to fatigue
- ? Emergency depts
- ? Anaesthesia/ Sedation
- ? COPD
**Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial**

<table>
<thead>
<tr>
<th>Randomisation</th>
<th>Paramedics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (high flow) (n=30)</td>
</tr>
<tr>
<td></td>
<td>Control (high flow) (n=226)</td>
</tr>
<tr>
<td></td>
<td>Patients excluded (n=109): No lung function data (n=103) FEV₁/FVC&gt;0.7 (n=6)</td>
</tr>
<tr>
<td></td>
<td>Subgroup with confirmed diagnosis of COPD</td>
</tr>
<tr>
<td></td>
<td>Patients included in ITT analysis (n=117)</td>
</tr>
<tr>
<td></td>
<td>Patients received non-protocol treatment (n=25; 21%)</td>
</tr>
<tr>
<td></td>
<td>Patients included in TPP analysis (n=92)</td>
</tr>
</tbody>
</table>
COPD – More is NOT better!

**WHAT IS ALREADY KNOWN ON THIS TOPIC**

Audits have shown increased mortality, acidosis, and hypercarbia in patients with acute exacerbations of chronic obstructive pulmonary disease treated with high flow oxygen.

High flow oxygen is still used routinely in prehospital and hospital areas for breathless patients with chronic obstructive pulmonary disease.

A “more is better” oxygen culture is strong in prehospital management.

**WHAT THIS STUDY ADDS**

Titrated oxygen treatment reduces mortality, acidosis, and hypercarbia in patients with acute exacerbation of chronic obstructive pulmonary disease treated before arrival at hospital.

The risk of death was reduced by 78% by use of titrated oxygen rather than high flow oxygen, with a number needed to harm of 14.

These findings provide strong evidence that titrated oxygen treatment should be used for hypoxic or breathless patients with chronic obstructive pulmonary disease in prehospital settings.

**Conclusions**

Titrated oxygen treatment significantly reduced mortality, hypercapnia, and respiratory acidosis compared with high flow oxygen in acute exacerbations of chronic obstructive pulmonary disease. These results provide strong evidence to recommend the routine use of titrated oxygen treatment in patients with breathlessness and a history or clinical likelihood of chronic obstructive pulmonary disease in the prehospital setting.
So ....lets avoid admission ?

• To assess the feasibility of employing the AIRVO system as an adjunct to conventional oxygen delivery systems in COPD patients by monitoring short-term physiological changes
Study Subjects

- Otherwise well, male COPD patients on home oxygen
- Able to breath through nose
- Ideally BMI <30

- Withdrawn if became anxious, tachypneic, $\text{SpO}_2$ fell by >10%
COPD Study N=30 Men- Home O$_2$ dependant

<table>
<thead>
<tr>
<th>Setup</th>
<th>Baseline</th>
<th>R1</th>
<th>Washout</th>
<th>R2</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mins</td>
<td>20 mins</td>
<td>20 mins</td>
<td>20 mins</td>
<td>20 mins</td>
<td>20 mins</td>
</tr>
</tbody>
</table>

R1 and R2 = randomised AIRVO or standard cannula
SpO₂

<table>
<thead>
<tr>
<th>Period</th>
<th>% of Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100</td>
</tr>
<tr>
<td>Standard</td>
<td>100</td>
</tr>
<tr>
<td>Washout</td>
<td>100</td>
</tr>
<tr>
<td>AIRVO</td>
<td>100</td>
</tr>
<tr>
<td>Recovery</td>
<td>100</td>
</tr>
</tbody>
</table>

p=ns
Heart Rate

![Heart Rate Graph](image)

- Baseline
- Standard
- Washout Period
- AIRVO
- Recovery

% of Baseline

p=ns

Critical Care Research Group
TcO$_2$ Dropped - ? A Cause for concern
Airvo and COPD

Transcutaneous $p\text{CO}_2$

% of Baseline

Standard

Period

AIRVO

Critical Care
RESEARCH GROUP
Respiratory Rate

![Respiratory Rate Graph]

- **Baseline**
- **Standard**
- **Washout**
- **AIRVO**
- **Recovery**

- **Period**

- **% of Baseline**
  - Baseline: 100%
  - Standard: 100%
  - Washout: 100%
  - AIRVO: < 100%
  - Recovery: > 100%

- **P-values**
  - Baseline to Standard: p<0.001
  - Standard to Washout: p<0.001
  - Washout to AIRVO: p<0.001
  - AIRVO to Recovery: p<0.001
  - Recovery to Baseline: p<0.0001

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Critical Care Research Group
Respiratory Rate

Transcutaneous CO2

Percent change from baseline

AIRVO  Washout  NP  Recovery

Critical Care
RESEARCH GROUP
Tidal Volume

Baseline AIRVO Washout Standard Recovery

p=0.0269

% of Baseline

Baseline Standard Washout Period AIRVO Recovery

p<0.001

p<0.05

p<0.001

p<0.05

p<0.05

p=0.0023

Critical Care RESEARCH GROUP
Minute Volume

Baseline AIRVO Washout Standard Recovery
80
90
100
110
120
Period
% of Baseline

Minute Volume

% of Baseline

Baseline Standard Washout AIRVO Recovery
80
90
100
110
120
Period

p=ns
AIRVO vs Nasal Prong  Video
Effects of Nasal High Flow on Ventilation in Volunteers, COPD and Idiopathic Pulmonary Fibrosis Patients

Respiration

Conclusions: nHF resulted in significant effects on respiratory parameters in patients with obstructive and restrictive pulmonary diseases. The rise in pressure amplitude and mean pressure and the decrease in breathing rate and minute volume will support inspiratory efforts, helps to increase effectiveness of ventilation and will contribute to a reduction in the work of breathing. A CO₂ wash-out effect in the upper airway part of the anatomical dead space may contribute to the beneficial effects of the nHF instrument.
Horses for courses
Conclusions – AIRVO and COPD...

• COPD
  – Respiratory rate is dropped
  – TCO2 drops
  – Increased TV seen

• AIRVO is generally well tolerated by these patients

• TcO$_2$ is reduced slightly when the same oxygen flow is entrained, but saturation is not
Paediatricians got there first..... 1986

**RELIEF OF SLEEP-RELATED OROPHARYNGEAL AIRWAY OBSTRUCTION BY CONTINUOUS INSUFLATION OF THE PHARYNX**

**Max Klein**  
**Louis G. Reynolds**

*Respiratory Service, Red Cross War Memorial Children’s Hospital,*  
*and Department of Paediatrics and Child Health, University of Cape Town, Cape Town.*

**COMPRESSED AIR**

**FLOW METER**

**HUMIDIFIER**

**INSUFLATION TUBE**

Fig 1—Method of continuous insufflation of the pharynx.

Orifice of nasopharyngeal tube is placed just beyond posterior edge of the soft palate, at entrance to oropharynx. Warm humidified air from compressed air source used.
Bernhard Frey · Peter J. McQuillan
Frank Shann · Nicholas Freezer

**Nasopharyngeal oxygen therapy produces positive end-expiratory pressure in infants**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Flow 1 (0.5 l/min)</th>
<th>Flow 2 (1.0 l/min)</th>
<th>Flow 3 (2.0 l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.0</td>
<td>6.1</td>
<td>10.6</td>
</tr>
<tr>
<td>2</td>
<td>3.3</td>
<td>2.8</td>
<td>4.0</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>-0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>4</td>
<td>2.0</td>
<td>2.2</td>
<td>1.4</td>
</tr>
<tr>
<td>5</td>
<td>1.0</td>
<td>1.5</td>
<td>2.4</td>
</tr>
<tr>
<td>6</td>
<td>2.3</td>
<td>4.1</td>
<td>3.1</td>
</tr>
<tr>
<td>7</td>
<td>0.5</td>
<td>-1.6</td>
<td>4.9</td>
</tr>
<tr>
<td>8</td>
<td>2.1</td>
<td>4.6</td>
<td>4.7</td>
</tr>
<tr>
<td>9</td>
<td>-1.1</td>
<td>6.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Mean</td>
<td>1.6</td>
<td>2.8</td>
<td>4.0</td>
</tr>
<tr>
<td>SD</td>
<td>1.4</td>
<td>2.7</td>
<td>2.9</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.7–2.5</td>
<td>1.0–4.6</td>
<td>2.1–5.9</td>
</tr>
<tr>
<td>$P^a$</td>
<td>0.008</td>
<td>0.014</td>
<td>0.004</td>
</tr>
</tbody>
</table>

$^a$Paired t-test versus baseline (no catheter and no flow)
Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery

Table 3 Infants with viral bronchiolitis listed by year

<table>
<thead>
<tr>
<th>Year</th>
<th>Total BRONCH</th>
<th>HF and HF + N</th>
<th>Total intubated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>52</td>
<td>7 (13%)</td>
<td>19 (37%)</td>
</tr>
<tr>
<td>2006</td>
<td>72</td>
<td>32 (44%)</td>
<td>21 (29%)</td>
</tr>
<tr>
<td>2007</td>
<td>49</td>
<td>23 (46%)</td>
<td>15 (31%)</td>
</tr>
<tr>
<td>2008</td>
<td>90</td>
<td>56 (62%)</td>
<td>12 (13%)</td>
</tr>
<tr>
<td>2009</td>
<td>67</td>
<td>44 (66%)</td>
<td>5 (7%)</td>
</tr>
</tbody>
</table>

2015: Current intubation rate ~3-5%
High-flow nasal cannula (HFNC) support in interhospital transport of critically ill children

![Graph showing percentage of retrievals over time with various methods of oxygen delivery]
Physiological Effect of HFNC in infants with Bronchiolitis
Change in Oesophagus Pressures

Pressure Rate Product (PRP) = Amp X RR

Pressure Time Product (PTP)

PEEPi
Neurally Adjusted Ventilatory Assist (NAVA)
NIV NAVA
17:28 Alarm: VT inspiratory overrange

O₂ cell calibration required

Trend graphs

on HFNC
off HNC

Cursor
Hours: 24
Close
Additional values
Diaphragm Activity on and off HFNC as a surrogate for Work of Breathing

Edi_max bronchiolitis and cardiac infants

Edi_ampl bronchiolitis and cardiac infants

Pham T. et al. Ped Pulmonolgy 2014
A RCT to investigate if high oxygen therapy has a lower failure rate vs standard oxygen in Bronchiolitis—in both regional and tertiary centres.

N = 1400 (580 already enrolled)
Sites: 17
Oxygen/Flow/Humidity

? What is the most important “bit”

- Is a Function of **Alveolar Surface**
  - *Size of the Lung, Atelectasis and Consolidation*

- Is a Function of **Shunt Fraction**
  - *ventilation-perfusion mismatch*

- Is a Function of **Ventilation Inhomogeneity**
  - *affected by Physiological Dead Space and preferential ventilation*

- Is a Function of **Alveolar-Capillary Membrane**
  - *Aa-Gradient*
Children’s Oxygen Administration Strategies Trial (COAST)

Kenya
Uganda
Niger
INTENSIVE CARE UNIT.

PLEASE WIPE OFF EXCESS MUD
Need for a trial?

• Optimal oxygen saturation threshold (currently recommends < 90%) for benefit - never tested in a controlled trial.

*Strong recommendation weak level of evidence*

• WHO suggests use of CPAP or non-invasive methods of respiratory support as a means of improving outcome

*Strong recommendation very weak level of evidence*
Predicting mortality: risk of death by $\text{SaO}_2$ at admission (n=36,036)

Inflection of risk $\sim$ 80%
Hypotheses to be tested

In 4200 children > 2 months with respiratory distress and hypoxia in 4 centres in Africa whether:

– Liberal oxygenation for $\text{SaO}_2 \geq 80\%$ will decrease mortality (at 48 hours & 28 days) Vs a strategy that includes permissive hypoxia (routine care);

– Use of high flow oxygen delivery will decrease mortality vs low flow oxygen delivery (routine care).
Conclusions

• Increasing understanding of the mechanism will assist in determining who can/cannot benefit from this technique

• Unclear which aspect is the most important

• Standardization of practice is essential to optimise outcomes
Acknowledgements

- Amanda Corley/ Amy Spooner and CCRG team
- Andreas and Donna Schibler
- Callum Spence
- Kath Maitland
- F and P
- Macquet
- NHMRC / Wellcome Trust / TPCH Foundnation