High Flow Oxygen Therapy in Acute Respiratory Failure

Laurent Brochard
Toronto
Conflicts of interest

• Our clinical research laboratory has received research grants for clinical research projects from the following companies:
  – Covidien (PAV+). Travel to Seoul.
  – Dräger (SmartCare)
  – General Electric (FRC)
  – Philips (NIV-sleep)
  – Fisher Paykel (High flow). Travel to Seoul.
  – To the Hospital: Maquet (NAVA)
Nasal High-Flow Oxygen Therapy

- High flows of inspired gas up to 60 L/min
- Full humidification (37 °C, 100 RH, 44 mg H₂O/L)
NHF: potential advantages

- Matching pt’s inspiratory flow (stable FiO2)
- CPAP effect (lung recruitment)
- Washout of nasopharyngeal deadspace
- Better humidification & comfort
Heated and Humidified High-Flow Oxygen Therapy Reduces Discomfort During Hypoxemic Respiratory Failure

Elise Cuquemelle MD, Tai Pham MD, Jean-François Papon MD PhD, Bruno Louis PhD, Pierre-Eric Danin MD, and Laurent Brochard MD PhD

\[ P = .004 \]

\[ P = .007 \]

\[ P = .03 \]

\[ P = .008 \]
Washout of nasopharyngeal dead space

The high gas flow decreases the upper airway dead space like trans-tracheal airway insufflation.
Nasal high flow clears anatomical dead space in upper airway models

Winfried Möller, Gülnaz Celik, Sheng Feng, Peter Bartenstein, Gabriele Meyer, Oliver Eickelberg, Otmar Schmid, and Stanislav Tatkov
NHF vs face mask after extubation

High-Flow Nasal Cannula Versus Conventional Oxygen Therapy After Endotracheal Extubation: A Randomized Crossover Physiologic Study

Nuttapol Rittayamai MD, Jamsak Tscheikuna MD, and Pitchayapa Rujiwit MD

17 pts after extubation
NHF vs non-rebreathing face mask for 30'

Rittayamai N, et al. Respir Care 2014;59:485–490
Nasal High-Flow oxygen therapy after extubation

No. 197 Assessed for Eligibility

No. 92 Excluded
  No. 68 Not Meeting Inclusion Criteria*
  No. 24 Refused to Participate

No. 105 Randomized

No. 53 Assigned to Receive NHF
  No. 53 Received NHF as Assigned
  No. 53 Included in Analysis
  No. 4 Post-Extubation Respiratory Failure
    No. 2 NIV
    No. 2 Success

No. 52 Assigned to Receive Venturi mask
  No. 52 Received Venturi mask as Assigned
  No. 52 Included in Analysis
  No. 18 Post-Extubation Respiratory Failure
    No. 8 NIV
    No. 7 Success

Maggiore SM et al. AJRCCM 2014;190:282-288
Nasal High-Flow oxygen therapy after extubation

Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation
Effects on Oxygenation, Comfort, and Clinical Outcome

Salvatore Maurizio Maggiore¹, Francesco Antonio Iodone¹, Rosanna Vaschetto², Rossano Festa³, Andrea Cataldo¹, Federica Antonicelli¹, Luca Montini¹, Andrea De Gaetano³, Paolo Navalesi⁴,⁵, and Massimo Antonelli¹

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* * * * NHF
Venturi mask

N intervention
N control
48 49 49 48 47 40 37
48 49 49 48 47 40 37

Discomfort related to the interface

Discomfort related to airway's dryness

Time (hours)

N intervention
N control
45 42 40 34 33 26 23
45 42 40 34 33 26 23

Maggiore SM et al. AJRCCM 2014;190:282-288
Nasal High-Flow oxygen therapy after extubation

**Nasal High-Flow versus Venturi Mask Oxygen Therapy after Extubation**
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With NHF:
- Fewer pts with interface displacements (32% vs 56%, \( p=0.01 \))
- Fewer pts with oxygen desaturations (40% vs 75%, \( p<0.01 \))

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<table>
<thead>
<tr>
<th>Condition</th>
<th>Control Group (( n=52 ))</th>
<th>NHF (( n=53 ))</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noninvasive ventilation, n (%)</td>
<td>8 (15.4)</td>
<td>2 (3.8)</td>
<td>0.042</td>
</tr>
<tr>
<td>Endotracheal intubation, n (%)</td>
<td>11 (21.2)</td>
<td>2 (3.8)</td>
<td>0.005</td>
</tr>
<tr>
<td>Cause of endotracheal intubation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercapnia with respiratory acidosis, n (%)</td>
<td>0</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Changes in mental status, n (%)</td>
<td>1 (1.9)</td>
<td>1 (1.9)</td>
<td>0.989</td>
</tr>
<tr>
<td>Oxygen desaturation or hypoxia, n (%)</td>
<td>6 (11.5)</td>
<td>1 (1.9)</td>
<td>0.047</td>
</tr>
<tr>
<td>Unbearable dyspnea with respiratory muscle failure, n (%)</td>
<td>4 (7.7)</td>
<td>1 (1.9)</td>
<td>0.162</td>
</tr>
<tr>
<td>Persistent hypotension, n (%)</td>
<td>2 (3.8)</td>
<td>0</td>
<td>0.149</td>
</tr>
<tr>
<td>Inability to clear secretions, n (%)</td>
<td>6 (11.5)</td>
<td>1 (1.9)</td>
<td>0.047</td>
</tr>
</tbody>
</table>

*Maggiore SM et al. AJRCCM 2014;190:282-288*
The RINO Trial
(ReINtubation rate after Oxygen therapy)

- Multicenter, randomized, controlled, phase III, open trial (NCT02107183)
- 500 patients
- Nasal high-flow vs Venturi mask after extubation
- Study hypothesis: using Optiflow for delivering oxygen therapy after extubation may reduce the extubation failure rate and the need for reintubation as compared with the Venturi mask
Flowchart of the study

Successful SBT (T-piece or PSV 7/0 for 30-120 min)

- Exhalation
  - Inclusion criteria: YES
  - Exclusion criteria: NO

- Randomization
  - Venturi mask
    1. O2 set to oxygenation target
  - Optiflow
    1. O2 set to oxygenation target
    2. Gas flow rate set at 5 L/min or according to O2's tolerance
    3. Humidifier set at 37°C or according to O2's tolerance

- Oxygenation target (SpO2): 92%-98%, (88%-95% if hypercapnia)

- Failure (ETI)
  - 72h or ICU discharge

- Success (no ETI)
  - ICU discharge

Inclusion criteria:
1. PaO2/FiO2 ≥ 300 (or SpO2/FiO2 ≥ 300 if SpO2 is lower than 96%) measured within 30 min. after extubation while breathing with Venturi mask (FiO2 30%)
2. Informed consent

Exclusion criteria:
1. Mechanical ventilation > 48 hr
2. Intubated
3. Prophylactic NIV *
4. Age < 18
5. Pregnancy

* Consecutive SBT failures > 3, pre-SBT PaCO2 > 45 mmHg with R<25/min

Duration of MV, adverse events, time from extubation to ICU discharge, ICU & hospital LOS, ICU readmission (with cause and timing), ICU & hospital mortality
Conclusions (I)

• Available data suggest that NHF is an effective method for delivering oxygen therapy:
  – better than conventional, low-flow devices in terms of gas exchange, respiratory rate, and comfort
  – safer than face mask, with less interface displacement and less oxygen desaturations

• NHF may play a role in protecting extubation and might improve clinical outcomes in patients with hypoxemic respiratory failure
**NHF in the ED**

*Humidified High Flow Nasal Oxygen During Respiratory Failure in the Emergency Department: Feasibility and Efficacy*

Hugo Lenglet MD, Benjamin Sztrymf MD, Christophe Leroy MD, Patrick Brun MD, Didier Dreyfuss MD, and Jean-Damien Ricard MD PhD

17 pts with hypoxemic ARF & dyspnea

<table>
<thead>
<tr>
<th></th>
<th>Before NHF</th>
<th>After 1h NHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borg scale</td>
<td>6</td>
<td>3 *</td>
</tr>
<tr>
<td>VAS dyspnea</td>
<td>7</td>
<td>3 *</td>
</tr>
<tr>
<td>RR, b/min</td>
<td>28</td>
<td>25 *</td>
</tr>
<tr>
<td>SpO2, %</td>
<td>90</td>
<td>97 *</td>
</tr>
</tbody>
</table>

NHF is feasible in the ED, and it alleviated dyspnea and improved respiratory parameters in subjects with hypoxemic ARF

*Lenglet H et al. Respir Care 2012;57:1873–1878*
NHF vs mask HF: improved success rate & compliance

A Preliminary Randomized Controlled Trial to Assess Effectiveness of Nasal High-Flow Oxygen in Intensive Care Patients

Rachael L Parke MHSc, Shay P McGuinness, and Michelle L Eccleston RN

60 pts with mild to moderate hypoxemic ARF
High-flow face mask vs NHF for 24 h

Fewer desaturations with NHF (15 vs 26)

Parke R, et al. Respir Care 2011;56:265-70
NHF in hypoxemic ARF

38 pts with ARF receiving NHF for 48h; 9 pts (24%) were intubated

Intubated pts (≈ at 1h):
- ↑ RR (30 vs 24 b/m)
- ↓ SpO2 (96 vs 98%)
- ↓ P/F ratio (91 vs 201)
- ↑ T/A asynchrony (75 vs 10% pts)

Acute Respiratory Failure
RR >25 c/min; PaO$_2$/FiO$_2$ ≤ 300, PaCO$_2$ <45 mmHg
Consent
(patient, Family, emergency)
Delay between random. and Tt <3 h
stratification on cardiac disease
NIV / $O_2$-HFH  $O_2$-HFH  $O_2$
(≥8h/d, $D_0$,$D_1$,$D_2$ min.) (24/24h, $D_0$,$D_1$,$D_2$ min.) (24h/24)
High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure

Jean-Pierre Frat, M.D., Arnaud W. Thille, M.D., Ph.D., Alain Mercat, M.D., Ph.D., Christophe Girault, M.D., Ph.D., Stéphanie Ragot, Pharm.D., Ph.D., Sébastien Perbet, M.D., Gwénaël Prat, M.D., Thierry Boulain, M.D., Elise Morawiec, M.D., Alice Cottereau, M.D., Jérôme Devaquet, M.D., Saad Nseir, M.D., Ph.D., Keyvan Razazi, M.D., Jean-Paul Mira, M.D., Ph.D., Laurent Argaud, M.D., Ph.D., Jean-Charles Chakarian, M.D., Jean-Damien Ricard, M.D., Ph.D., Xavier Wittebole, M.D., Stéphanie Chevalier, M.D., Alexandre Herbland, M.D., Muriel Fartoukh, M.D., Ph.D., Jean-Michel Constantin, M.D., Ph.D., Jean-Marie Tonnelier, M.D., Marc Pierrot, M.D., Armelle Mathonnet, M.D., Gaëtan Béduneau, M.D., Céline Delétage-Météreau, Ph.D., Jean-Christophe M. Richard, M.D., Ph.D., Laurent Brochard, M.D., and René Robert, M.D., Ph.D., for the FLORALI Study Group and the REVA Network*
Patients were admitted to the ICUs in the study period, February 2011-April 2013. 4777 With Acute Respiratory Failure. 2506 With de novo Acute Respiratory Failure. Patients with ARF were excluded because:
- Acute on chronic lung disease (1366)
- Cardiogenic pulmonary edema (651)
- NIV contraindications (155)
- For administrative reasons (99)

Patients with de novo ARF were excluded because:
- Shock or coma Glasgow scale <12 (647)
- Hypercapnia (PaCO₂ >45 mmHg) (582)
- Urgent need for intubation (476)
- “Do Not Intubate” order (180)
- Neutropenia (96)

525 Were eligible. 313 Underwent randomization. 106 Were assigned to High-Flow Oxygen group. 96 Were assigned to Standard Oxygen group. 111 Were assigned to NIV group. 1 Patient withdrew consent.

310 Were included in the analysis and in the 90-day follow up. 106 Were in the High-Flow Oxygen group. 94 Were in the Standard Oxygen group. 110 Were in the NIV group.

160 Were not included for logistical reasons. 52 Patients refused to participate.
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age – yr</td>
<td>61±16</td>
<td>59±17</td>
<td>61±17</td>
</tr>
<tr>
<td>Male sex – no. (%)</td>
<td>75 (70.7)</td>
<td>63 (67.0)</td>
<td>74 (67.3)</td>
</tr>
<tr>
<td>Body-mass index†</td>
<td>25±5</td>
<td>26±5</td>
<td>26±6</td>
</tr>
<tr>
<td>SAPS II at inclusion§</td>
<td>25±9</td>
<td>24±9</td>
<td>27±9</td>
</tr>
<tr>
<td>SOFA at inclusion¶</td>
<td>3.7±2.0</td>
<td>3.6±1.8</td>
<td>4.2±2.1</td>
</tr>
<tr>
<td>Preexisting cardiac failure – no. (%)</td>
<td>8 (7.5)</td>
<td>4 (4.3)</td>
<td>8 (7.3)</td>
</tr>
<tr>
<td>Immunodeficiency – no. (%)</td>
<td>26 (24.5)</td>
<td>30 (31.9)</td>
<td>26 (23.6)</td>
</tr>
<tr>
<td>Smoker – no. (%)</td>
<td>34 (32.1)</td>
<td>36 (38.3)</td>
<td>40 (36.4)</td>
</tr>
<tr>
<td>Reason for acute respiratory failure – no. (%) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>71 (67.0)</td>
<td>57 (60.6)</td>
<td>69 (62.7)</td>
</tr>
<tr>
<td>Hospital-acquired pneumonia</td>
<td>12 (11.3)</td>
<td>13 (13.8)</td>
<td>12 (10.9)</td>
</tr>
<tr>
<td>Other</td>
<td>23 (21.7)</td>
<td>24 (25.6)</td>
<td>29 (26.4)</td>
</tr>
<tr>
<td>Bilateral pulmonary infiltrates – no. (%)</td>
<td>79 (74.5)</td>
<td>80 (85.1)</td>
<td>85 (77.3)</td>
</tr>
<tr>
<td>Clinical parameters</td>
<td>Value 1</td>
<td>Value 2</td>
<td>Value 3</td>
</tr>
<tr>
<td>-------------------------------------------</td>
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<tr>
<td><strong>Respiratory rate - breaths/min</strong></td>
<td>33±6</td>
<td>32±6</td>
<td>33±7</td>
</tr>
<tr>
<td><strong>Heart rate - beats/min</strong></td>
<td>106±21</td>
<td>104±16</td>
<td>106±21</td>
</tr>
<tr>
<td><strong>Systolic arterial pressure – mm Hg</strong></td>
<td>127±24</td>
<td>130±22</td>
<td>128±21</td>
</tr>
<tr>
<td><strong>Mean arterial pressure – mm Hg</strong></td>
<td>87±17</td>
<td>89±15</td>
<td>86±16</td>
</tr>
<tr>
<td><strong>Arterial blood gas</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>7.43±0.05</td>
<td>7.44±0.06</td>
<td>7.43±0.06</td>
</tr>
<tr>
<td><strong>PaO₂ – mm Hg</strong></td>
<td>85±31</td>
<td>92±32</td>
<td>90±36</td>
</tr>
<tr>
<td><strong>FiO₂</strong></td>
<td>0.62±0.19</td>
<td>0.63±0.17</td>
<td>0.65±0.15</td>
</tr>
<tr>
<td><strong>PaO₂:FiO₂ ratio – mm Hg</strong></td>
<td>157±89</td>
<td>161±73</td>
<td>149±72</td>
</tr>
<tr>
<td><strong>PaCO₂ – mm Hg</strong></td>
<td>36±6</td>
<td>35±5</td>
<td>34±6</td>
</tr>
</tbody>
</table>
Cumulative incidence of Being Intubated in the Overall Population

Number at risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Days After Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Flow Oxygen group</td>
<td>106  68  67  67  65  65  65  65</td>
</tr>
<tr>
<td>Standard Oxygen group</td>
<td>94   52  50  49  49  49  48  48</td>
</tr>
<tr>
<td>NIV group</td>
<td>110  64  57  53  53  53  53  52</td>
</tr>
</tbody>
</table>

P=0.17 by log-rank test
Cumulative Incidence of Being Intubated in the Patients With a PaO₂:FiO₂ ≤ 200 mm Hg

Number at risk

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
<th>28</th>
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</thead>
<tbody>
<tr>
<td>High-Flow Oxygen group</td>
<td>83</td>
<td>55</td>
<td>54</td>
<td>54</td>
<td>53</td>
<td>53</td>
<td>53</td>
<td>53</td>
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<tr>
<td>Standard Oxygen group</td>
<td>74</td>
<td>37</td>
<td>35</td>
<td>34</td>
<td>34</td>
<td>34</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>NIV group</td>
<td>81</td>
<td>41</td>
<td>34</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
</tbody>
</table>

P=0.009 by log-rank test
Kaplan-Meier Plot of the Probability of Survival from Randomization to Day 90

Cumulative Probability of Survival

Days After Enrollment

P = 0.015 by log-rank test

Number at risk

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>75</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Flow Oxygen group</td>
<td>106</td>
<td>100</td>
<td>97</td>
<td>94</td>
<td>94</td>
<td>93</td>
<td>93</td>
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<tr>
<td>Standard Oxygen group</td>
<td>94</td>
<td>84</td>
<td>81</td>
<td>77</td>
<td>74</td>
<td>73</td>
<td>72</td>
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<tr>
<td>NIV group</td>
<td>110</td>
<td>93</td>
<td>86</td>
<td>80</td>
<td>79</td>
<td>78</td>
<td>77</td>
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<tr>
<td></td>
<td>High-Flow Oxygen group (n=106)</td>
<td>Standard Oxygen group (n=94)</td>
<td>NIV group (n=110)</td>
<td>P Value</td>
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<tr>
<td>Respiratory patient-discomfort at inclusion – mm †</td>
<td>38±31</td>
<td>44±29</td>
<td>46±30</td>
<td>0.20</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Respiratory patient-discomfort at H1– mm ‡</td>
<td>29±26</td>
<td>40±29</td>
<td>43±29</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
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<tr>
<td>Grade of dyspnea at H1‡</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marked improvement – no. (%)</td>
<td>19 (22.1)</td>
<td>5 (6.8)</td>
<td>13 (14.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Slight improvement– no. (%)</td>
<td>46 (53.5)</td>
<td>26 (35.1)</td>
<td>40 (44.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No change– no. (%)</td>
<td>18 (20.9)</td>
<td>33 (44.6)</td>
<td>23 (25.3)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Slight deterioration – no. (%)</td>
<td>3 (3.5)</td>
<td>9 (12.2)</td>
<td>8 (8.8)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Marked deterioration – no. (%)</td>
<td>0 (0.0)</td>
<td>1 (1.3)</td>
<td>7 (7.7)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Respiratory rate– breaths/min</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H1</td>
<td>28±7</td>
<td>31±7</td>
<td>31±8</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H6</td>
<td>27±7</td>
<td>29±8</td>
<td>29±7</td>
<td>0.13</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusions (II)

• Humidification is important in airway management
• High flow systems may provide optimal humidification and may reduce dead space
• These well tolerated systems may become the first line therapy in hypoxemic respiratory failure