Nitric Oxide

Biological Rationale

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Disclosures

Member of steering committee for clinical trial in PAH - Ikaria
The Nobel Prize in Physiology or Medicine
1998

Robert F. Furchgott
Prize share: 1/3

Louis J. Ignarro
Prize share: 1/3

Ferid Murad
Prize share: 1/3
L-arginine → NOS → L-citruline + H_2O + NADP^+ → ONOO^•

O_2 + NADPH → O_2^- + GTP → Cyclic GMP → sGC
Satisfies the criteria of a good pulmonary vasodilator

Selective (PVR vs SVR)
Rapid onset of action
Short half life
Good side effect profile
? Cost
Rationale

• Improve gas exchange
INHALED NITRIC OXIDE FOR THE ADULT RESPIRATORY DISTRESS SYNDROME

Rolf Rossaint, M.D., Konrad J. Falke, M.D., Frank López, B.S., Klaus Slama, M.D., Ulrich Pison, M.D., and Warren M. Zapol, M.D.
Rationale

• Improve gas exchange

• Reduce intensity of mechanical ventilation

• Alter inflammatory response
Other therapeutic properties of iNO

Reduction of PMN influx after IR injury

Inhibits neutrophil activation, aggregation and migration

Inhibits platelet aggregation
   (Radomski Proc National Acad Science. 1990;87:5193-5197)

Reduces adhesion molecule expression

Regulates apoptosis
NO in reperfusion injury (PGD)

Protects graft function

- reduced neutrophil sequestration
- reduces endothelial dysfunction

reduces pulmonary pressure
improves oxygenation
A Randomized Trial of Inhaled Nitric Oxide to Prevent Ischemia–Reperfusion Injury after Lung Transplantation

Maureen O. Meade, John T. Granton, Andrea Matte-Martyn, Karen McRae, Bruce Weaver, Paula Cripps, Shaf H. Keshavjee, and the Toronto Lung Transplant Program

Toronto Lung Transplant Program, Toronto General Hospital, University of Toronto; and Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada

### TABLE 2. POSTOPERATIVE EVENTS

<table>
<thead>
<tr>
<th>Event</th>
<th>NO Group (n = 42)</th>
<th>Control Group (n = 42)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{Pa}_2/\text{Fi}_2) &lt; 150 in first 48 h</td>
<td>9 (22.0%)</td>
<td>8 (19.0%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Unblinded NO initiated in ICU</td>
<td>2 (4.9%)</td>
<td>1 (2.4%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Time to unassisted breathing, h</td>
<td>25.7 (10.8–75.3)</td>
<td>27.3 (12.9–267.1)</td>
<td>0.76</td>
</tr>
<tr>
<td>Time to successful extubation, h</td>
<td>28.5 (15.8–135.0)</td>
<td>35.3 (18.5–130.5)</td>
<td>0.86</td>
</tr>
<tr>
<td>Time to ICU discharge, d</td>
<td>3.0 (3.0–7.5)</td>
<td>3.0 (3.0–16.5)</td>
<td>0.90</td>
</tr>
<tr>
<td>Time to hospital discharge, d</td>
<td>26.8 (21.5–37.7)</td>
<td>29.3 (19.8–46.6)</td>
<td>0.56</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In operating room</td>
<td>1/42 (2.4%)</td>
<td>0/42 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>In ICU before first extubation</td>
<td>3/41 (7.3%)</td>
<td>3/42 (7.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>In ICU after first extubation</td>
<td>1/38 (2.6%)</td>
<td>1/39 (2.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>In hospital after ICU discharge</td>
<td>0/37 (0.0%)</td>
<td>2/38 (5.3%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Total</td>
<td>5/42 (11.9%)</td>
<td>6/42 (14.3%)</td>
<td>0.75</td>
</tr>
<tr>
<td>30-d postoperative mortality</td>
<td>4/42 (9.5%)</td>
<td>5/42 (11.9%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Rationale for use in PH / PAH

• Acute vasodilator challenge
• Salvaging the RV
  • PAH crisis
  • Post heart transplantation
  • Post lung transplantation
  • Massive PE
Inhaled NO as a Viable Antiadhesive Therapy for Ischemia/Reperfusion Injury of Distal Microvascular Beds

Alison Fox-Robichaud,‡ Derrice Payne,† Shabih U. Hasan,§ Lena Ostrovsky,⁎ Todd Fairhead,† Paul Reinhardt,† and Paul Kubes†

⁎Immunology Research Group, †Division of Critical Care, and the §Respiratory Research Group, University of Calgary, Calgary, Alberta, T2N 4N1, Canada
the most important discovery in cardiovascular medicine