Permissive hypoxaemia

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Thursday, 28 April 2011
Is mechanical ventilation such a good idea?

- ventilator-induced lung injury (short- & long-term)
- systemic effects
  - → immune activation, cardiovascular effects
- need for sedation
  - → immunosuppression, cardiovascular effects
- ventilator-associated pneumonia
Recent paradigms

ALI → ARDS

'bad ARDS'

HFO
Novolung
ECMO
ECCO$_2$R...

IR-PCV..
permissive hypercapnia
prone positioning...

mode variants, posture...

NO,
surfactant
fluorocarbon...

Permissive hypoxaemia

Permissive hypoxaemia
Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial

Giles J Peek, Miranda Mugford, Ravindranath Tiruvoipati, Andrew Wilson, Elizabeth Allen, Mariamma M Thalanchy, Clare L Hibbert, Ann Truesdale, Felicity Clemens, Nicola Cooper, Richard K Firmin, Diana Elbourne, for the CESAR trial collaboration


Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome

JAMA. 2009;302
.. but what about complications?

Hemorrhagic complications occurred in 37 patients (54%) during ECMO therapy, with the most common sources being ECMO cannulation sites in 15 patients (22%), gastrointestinal tract in 7 patients (10%), respiratory tract in 7 patients (10%), vaginal bleeding in 6 patients (9%), and intracranial hemorrhage in 6 patients (9%).

Infected complications occurred in 42 patients (62%) during ECMO therapy, with the most common sites being respiratory tract in 30 patients (44%), bloodstream in 14 patients (21%), non-ECMO catheter-related in 13 patients (19%), and ECMO cannulae-related in 7 patients (10%).

What's the long-term morbidity?

- stroke?
- leg amputation?
- neurocognitive disturbances? ...
“I never inhaled …”

OXYGEN ENEMATA AS A REMEDY IN CERTAIN DISEASES OF THE LIVER AND INTESTINAL TRACT
Kellogg JH, JAMA, 1888

THE INTRAVENOUS INJECTION OF OXYGEN GAS AS A THERAPEUTIC MEASURE
Tunnicliffe, FW, Stebbing GF. Lancet 1916 (ii) 321-3
THE INTRAVENOUS INJECTION OF OXYGEN GAS AS A THERAPEUTIC MEASURE.

By F. W. Tunnicliffe, M.D. Lond.,
Physician, King’s College Hospital; Lecturer on Therapeutics,
King’s College Hospital Medical School;

And

G. F. Stebbing, M.B., B.S. Lond.,
Assistant Medical Officer, Lambeth Infirmary.

There must occur to clinicians instances in which the relief by the intravenous injection of oxygen of an acute cyanosis, either unrelieved or from the nature of the case impossible to relieve by the inhalation of the gas, might be of very considerable therapeutic value.

The result of our observations is that oxygen gas can be introduced into the veins in quantities from 500 to 1000 c.c. at the rate of from 600 to 1200 c.c. per hour. Cyanosis and the dyspnoea attending it are rapidly relieved; the rate we usually begin with is 500 c.c. per hour. The more cyanosed the patient, the better is a rapid rate tolerated. As the cyanosis is reduced the rate should be diminished.
Supplemental Systemic Oxygen Support Using an Intestinal Intraluminal Membrane Oxygenator


results show that it is possible to meet a physiologically significant portion of the body’s O₂ demands via the intestine during respiratory hypoxia and suggests that similar devices may be of significant potential value as a supplemental oxygenation device in cases of respiratory distress.

**FIG. 2.** Shown is O₂ content as percent of baseline for SMV (A), mixed venous blood (B), and arterial blood (C).

FiO₂ 0.14
What about permissive hypoxaemia?
Case history (i)

- 23 y.o. male
- overdose of anti-epileptics
- Rx: activated charcoal in local hospital ER
  ---> aspirated charcoal ---> severe lung injury
- after 10d ---> UCLH ICU with ARDS and multiple bronchopleural fistulae
- PC ventilation (24 + 16 PEEP), FiO$_2$ 1.0
- SaO$_2$ 88%, PaO$_2$ 7 kPa, PaCO$_2$ 10.2 kPa
- also requiring norepinephrine

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Early May
Late May

PC ventilation
(20 + 10 PEEP)
FiO₂ 1.0
SaO₂ 73%
PaO₂ 4.7 kPa
PaCO₂ 14 kPa
surgeons not interested

off inotropes
Kidneys OK
Late June

weaning!
Late July

extubated!

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Case history (ii)

35 y.o. female

- collapse, SOB during epidural pre-Caesarean section
- urgent intubation for severe hypoxaemia
- CXR: ARDS
- Rx: high FiO$_2$, PEEP, IR-PCV
- improved by Day 3: FiO$_2$ 0.6, PaO$_2$ 8 kPa
- plateau’d for 4 days, then gradual decline

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Day 13:

- FiO$_2$ 1.0
- PEEP 14
- IR-PCV (PAP 45 cm H$_2$O)
- prone positioning
- PaO$_2$ 3.8 kPa, SaO$_2$ 66%
- pneumothorax

--- referred to UCLH
On arrival:

- **SaO₂ 68%**
- yet all other organ systems **working**
- **CO 8 l/min, BP 110/60**
- **P.U.’ing 50-80 ml/hr**
- liver function tests normal
- base excess +5.4, **PaCO₂ 8.3 kPa**
transferred without problem
slow but steady improvement
day 35: discharged ICU
day 48: discharged home
last seen pushing 3 kids round supermarket
Have they both ‘acclimatised’???
Effects of altitude (low $\text{PaO}_2$) on performance

- Weakness
- Coma within minutes at rest
- Coma on exertion
- Unreliable
- Poor learning
- Death

$\text{PO}_2$ (kPa) vs. altitude ($x \times 10^3 \text{ ft}$)

Thursday, 28 April 2011
Arterial Blood Gases and Oxygen Content in Climbers on Mount Everest

Michael P.W. Grocott, M.B., B.S., Daniel S. Martin, M.B., Ch.B.,
Denny Z.H. Levett, B.M., B.Ch., Roger McMorow, M.B., B.Ch.,
Jeremy Windsor, M.B., Ch.B., and Hugh E. Montgomery, M.B., B.S., M.D.,
for the Caudwell Xtreme Everest Research Group*

Table 2. Arterial Blood Gas Measurements and Calculated Values for Pulmonary Gas Exchange from Four Subjects at an Altitude of 8400 m, during Descent from the Summit of Mount Everest.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subject No.</th>
<th>Group Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>pH</td>
<td>7.55</td>
<td>7.45</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)†</td>
<td>29.5</td>
<td>19.1</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)†</td>
<td>12.3</td>
<td>15.7</td>
</tr>
<tr>
<td>Bicarbonate (mmol/liter)‡</td>
<td>10.5</td>
<td>10.67</td>
</tr>
<tr>
<td>Base excess of blood†</td>
<td>-6.3</td>
<td>-9.16</td>
</tr>
<tr>
<td>Lactate concentration (mmol/liter)‡</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>SaO₂ (%)†</td>
<td>68.1</td>
<td>34.4</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)‡</td>
<td>20.2</td>
<td>18.7</td>
</tr>
<tr>
<td>Respiratory exchange ratio¶</td>
<td>0.81</td>
<td>0.74</td>
</tr>
<tr>
<td>PaO₂ — mm Hg†**</td>
<td>32.4</td>
<td>26.9</td>
</tr>
<tr>
<td>Alveolar–arterial oxygen difference — mm Hg†</td>
<td>2.89</td>
<td>7.81</td>
</tr>
</tbody>
</table>

Hypoxia response systems

* carotid body $O_2$ sensors
  --> hypoxic ventilatory response (HVR)
* pulmonary vascular $O_2$ sensors
  --> hypoxic pulmonary vasoconstriction
* peripheral $O_2$ sensors
  --> hypoxic vasodilation (via NO, nitrite...)
  --> expression of VEGF (+ receptors) -> angiogenesis
* $O_2$ sensors in kidney/liver
  --> erythropoietin ----> increased RBC mass
* tissue-specific $O_2$ sensing & signal transduction pathways
  --> altered expression of hypoxia-sensitive genes
  for metabolic enzymes & transporters
Adaptation to altitude

circulatory response:
* global changes
* regional changes (flow and pressure)

respiratory response:
* minute ventilation
* \( V/Q \)

vascular response:
* polycythaemia
* ↑ tissue capillarity
* oxyHb curve shift

cellular response:
* ↑ myoglobin
* ↑ mitochondrial density
* ↑ resp’y enzyme activities
* metabolic changes
* phenotype changes (e.g. fast --＞ slow twitch fibres)
Adaptation to exercise

Hochachka PNAS 1998; 95: 1915-20
Arterial-mitochondrial PO$_2$ gradient

oxygen tension (kPa)

- Artery
- Capillary
- Interstitium
- Cell
- Mitochondria

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We cope, we adapt………

- mountaineers
- altitude dwellers
- pearl fishers
- Type II chronic bronchitics
- congenital cyanotic heart disease
- .. how about sepsis & ARDS???
Conclusions

- consider permissive hypoxaemia for severe ARDS as a better alternative to ‘driving’ ventilation, mechanical supports, etc..
- allow time (1-2 weeks?) to ‘acclimatise’ slowly
- carefully monitor adequacy of organ perfusion