Ventilation strategies in ARDS

Sawsan Alyousef MD FCCP
Pediatric Intensivist
Assistant head of PICU
Head of simulation centre
Security Forces Hospital
American-European consensus 1994

• **ARDS**: acute respiratory distress syndrome
criteria:
  • Acute onset
  • Bilateral infiltrates on chest radiograph
  • Exclusion of left Atrial hypertension
  • Two categories:
    - Acute Lung Injury - $\text{PaO}_2/\text{FiO}_2$ ratio $\leq 300$
    - ARDS - $\text{PaO}_2/\text{FiO}_2$ ratio $\leq 200$
Possible etiology

**Direct Injury**
- **Common Causes**
  - Pneumonia 28%
  - Gastric aspiration 14%
- **Less Common Causes**
  - Pulmonary contusion
  - Fat emboli
  - Near drowning
  - Inhalational injury

**Indirect Injury**
- **Common Causes**
  - Sepsis 32%
  - Shock after severe trauma 5%
- **Less Common Causes**
  - Cardiopulm. Bypass
  - Drug overdose
  - Acute pancreatitis
  - Massive blood transfusions

Davis et al., J Peds 1993;123:35
STAGES

• **Acute, exudative-inflammatory phase**
  - rapid onset of respiratory failure after trigger
  - diffuse alveolar damage with inflammatory cell infiltration
  - hyaline membrane formation
  - capillary injury
  - protein-rich edema fluid in alveoli
  - disruption of alveolar epithelium
STAGES

- Subacute, Proliferative phase: 4-10 days
  - persistent hypoxemia
  - development of hypercarbia
  - further decrease in pulmonary compliance
  - pulmonary hypertension
STAGES

• **Chronic phase above 10 days**
  - fibrosing alveolitis
  - obliteration of alveolar and bronchiolar spaces and pulmonary capillaries

• **Recovery phase**
  - gradual resolution of hypoxemia
  - improved lung compliance
  - resolution of radiographic abnormalities
Normal Alveolus

(Adapted from the ICU Book by P. Marino)
ACUTE PHASE OF ARDS

(Adapted from the ICU Book by P. Marino)
Pathophysiology

- Abnormalities of gas exchange
- Oxygen delivery and consumption
- Cardiopulmonary interactions
- Multiple organ involvement
Abnormalities in Gas Exchange

• Hypoxemia: HALLMARK of ARDS
  - Increased capillary permeability
  - Interstitial and alveolar exudate
  - Surfactant damage
  - Decreased FRC
  - Diffusion defect and right to left shunt
Oxygen delivery and consumption

\[ \text{VO}_2 = \text{DO}_2 \times \text{O}_2\text{ER} \]

Normal

Septic Shock/ARDS
Abnormal Flow Dependency
Cardiopulmonary interactions

- A = Pulmonary hypertension resulting in increased RV afterload
- B = Application of high PEEP resulting in decreased preload
- A+B = Decreased cardiac output
Respiratory support

- **Goal**: maintain sufficient oxygenation and ventilation, minimize complications of ventilatory management
ARDS therapies

Innovations:
- iNO
- PLV
- Proning
- Surfactant
- Anti-Inflammatory

Gentle ventilation:
- Permissive hypercapnia
- Low tidal volume
- Open-lung
- HFOV

ARDS

ECMO
Lung Protection strategy

- Implemented immediately on intubation
- Limit tidal volume 6-8 ml/kg
- PEEP above inflection point
- FiO2 <0.6 and saturation (88-90%)
- Permissive hypercapnia

NIH study NEJM 2000;342:1301-8
Lung protective strategies

- Multi-center trial, 861 adult ARDS
- Randomized:
  - Tidal volume 12 cc/kg
    Plateau pressure < 50 cm H2O
  vs.
  - Tidal volume 6 cc/kg
    Plateau pressure < 30 cm H2O

ARDS Network, NEJM, 342: 2000
• Mortality was 39.8% — 31%
• Ventilatory free days was higher in LPS
Open lung ventilation technique

Advantages of high PEEP to
- Recruit more alveoli
- Reduce atelactasis
- Reduce stretch sheering injury

Disadvantages
- Reduces cardiac output
- Increases airway pressure
Comparing High Vs low PEEP

- Brower et al NEJM 2004 351:327-336

No difference in
- mortality
- number of ventilatory free days
- incidence of multiorgan failure
Airway Pressure (cmH₂O)

Lung Volume (ml/kg)

atelectases  Preferred area  Over distension
Strategies on HFO

- Rapid rate
- Low tidal volume
- Maintain open lung
- Minimal volume swings
HFO in Paediatric

- Total of 290 patient, not blinded study
- Greater survival without severe lung disease
- Greater crossover to HFOV and improvement
- Failure to respond to HFOV strong predictor of death

Arnold et al, CCM, 1994
HFO

- Dobyns et al, Jped.2000

58% was the survival rate for both HFO group and CMV group

For adults: HFO benefits have not been proven

Further prospective RCT are required
Inhaled Nitric Oxide

- Pulmonary vasodilator
- Selectively improves perfusion of ventilated areas
- Reduces intrapulmonary shunting
- Improves arterial oxygenation
Inhaled Nitric Oxide

- Inhaled Nitric Oxide Study Group
  - Prospective, randomized, placebo controlled, double blinded, multi-center study
  - 177 adults with ARDS
  - Improvement in oxygenation index
  - No significant differences in mortality or days off ventilator

Inhaled Nitric Oxide

• First paediatric study was 1990s by Abman et al followed by several studies and all showed:
  • iNO is helpful as short term in ARDS as it improves Oxygenation
  • There were no difference in survival rate
Surfactant AND ARDS

- Surfactant deficiency
- Surfactant present is dysfunctional
  - Surfactant replacement improves physiologic function
Surfactant in ARDS

- Multicenter trial-uncontrolled, observational
- Calf lung surfactant (Infasurf) - intratracheal
- Immediate improvement and weaning in 24/29 children with ARDS and 14% mortality

Wilson et al, CCM, 24:1996
Surfactant in ARDS

• In several other studies, there is no evidence for sustained benefit from Surfactant administration

   Wilson et al, *JAMA*, 2005

Exogenous surfactant is more active and has greater efficacy in direct lung injury as opposed to indirect lung injury

Exogenous surfactant

- Exosurf ARDS Sepsis Study. Anzueto et al. NEJM 1996;334:1417-21
  - Randomized control trial
  - Multicenter study of 725 adult patients with sepsis induced ARDS
  - No significant difference in oxygenation, duration of mechanical ventilation, hospital stay, or survival
Prone position

- Improved gas exchange
- More uniform alveolar ventilation
- Recruitment of atelectasis in dorsal regions
- Improved postural drainage
- Redistribution of perfusion away from edematous, dependent regions
Prone position

- Observational study of 39 patients with ARDS in different stages
- Improved oxygenation in prone (PaO₂/FiO₂ 189±34 prone vs. 83±14 supine) after 6 hours
- No improvement in patients with late ARDS or pulmonary fibrosis

Nakos G et al. Am J Respir Crit Care Med 2000;161:360-68
Prone position

- Prone-Supine Study Group
- Multicenter randomized clinical trial
- 304 adult patients prospectively randomized to 10 days of supine vs. prone ventilation 6 hours/day
- Improved oxygenation in prone position
- No improvement in survival

NEJM 2001;345:568-73
Partial Liquid Ventilation (PLV)

- Ventilating the lung with conventional ventilation after filling with perfluorocarbon
- Perfluorocarbon
  - 20 times $O_2$ and 3 times the $CO_2$ solubility
  - Heavier than water
  - Higher spreading coefficient
  - Studies in animal models suggest improved compliance and gas exchange
Partial Liquid Ventilation (PLV)

- RCT was aborted in pediatric population
- RCT in adult improve gas exchange with minimal complications
- Need more trials
Indications for ECMO in Paediatric

- Potential candidates
- Neonate - 18 years
- Reversible disease process
- Severe respiratory/cardiac failure
- < 10 days mechanical ventilation
- Acute, life-threatening deterioration
Impact of ECMO on Survival in Pediatric Respiratory Failure

- Retrospective, multicenter cohort analysis
- 331 patients, 32 hospitals (with predicted mortality 50-75%)
- Use of ECMO associated with survival (p < .001)
- 53 diagnosis and risk-matched pairs: ECMO decreased mortality (26% vs 47%)
- Incidence of CNS bleeds is high

-Green et al, CCM, 24:1996
Anti inflammatory strategies

- Glucocorticoid therapy
- Prostaglandin $E_1$
- Antioxidant therapy RCT failed to show improvement
- Anti IL-8 therapy need further studies
Corticosteroids in the Fibroproliferative Stage

- 24 patients with severe ARDS and failure to improve by day 7 of treatment
- Placebo vs. methylprednisolone 2mg/kg/day for 32 days
- Steroid group showed improvement in lung injury score, improved oxygenation, reduced mortality
- No significant difference for early or late corticosteroid

Meduri GU et al. JAMA 1998;280:159-65
Inhaled Aerosolized Prostaglandin E1 (IAP)

- Potent selective pulmonary vasodilator
- Effective for pulmonary hypertension
- Short half-life (2-3 min) with rapid clearance
- Little or no hemodynamic effect
- Randomized clinical trials have not been done
Summary

- Low tidal volumes: Outcome benefit in large study
- Prone positioning: Unproven outcome benefit
- Open-lung strategy: Outcome benefit in small study
- HFOV: Outcome benefit in small study
- ECMO: Proven in neonates, unproven in children
Summary

- Surfactant: possible benefit in children
- Inhaled NO: no benefit
- PLV: no benefit
Thank You!