EXOGENOUS SURFACTANT SUPPLEMENTATION

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Pulmonary surfactant functions

- Lowers surface tension at air-liquid interface
- Breaths with minimal effort
- Protects patency of small airways and alveolus
- Prevents movements of fluid into the alveolus
- Enhances mucous clearance
- Stimulates lung host defence system

Surfactant activities in normal lung and ARDS

Normal lung	***ARDS***
<u>Surfactant activities</u>	<u>Surfactant deficiency</u>
Reduce alveolar surface tension Stabilise alveolar volume	Alveolar collapse
Prevents movements of fluid into alveolus	Alveolar oedema
Protects patency of small airways	Increased resistence to airflow through small airways

Pulmonary surfactant composition

80% phospholipids

- Dipalmitoylphosphatidylcholine DPPC (60%)
- Phosphatidyl glycerol / ethanolamine / inositol (20%)

10% neutral lipids

- Mostly cholesterol

10% Surfactant proteins

- SP-A, SP-D: hydrophilic
- SP-B, SP-C: hydrophobic

Pulmonary surfactant physiology

- Surfactant is produced, stored and secreted by alveolar type II cells and Clara cells
- Half-time for turnover in animals is 5 to 10 hrs
- 90% of surfactant is recycled by pneumocytes type II and 10% is cleared by alveolar macrophages
- SP-A is a primary regulator of metabolism and lungs' defense mechanisms

Loss of surfactant biophysical function

- Inhibition by plasma proteins (fibrin and degradation products, albumin)
- Inactivation by oxygen radicals and enzymes (phospholipases)
- Mechanical factors: alveolar collapse
- Enhanced conversion to small aggregate forms of lipids
- Decrease pool size from different lung injury

Available surfactants on the market for clinical use

Natural
Bovine (Survanta®, Infasurf®, Alveofact®)
Porcine (Curosurf®)
Synthetic
Without proteins (Exosurf®)
With proteins (KL4®, Venticute®)

Surfactant delivery techniques
1. Bolus instillation
2. Aerosolization
3. Selective bronchial instillation

Bolus instillation
Advantages
Large dose
Rapid delivery
Rapid response

Disadvantages
Not uniform distribution
Liquid bolus
Obstruction (tube, airways)

Aerosolization

Advantages

Uniform distribution
"gentle administration"
Direct alveolar administration
Reduced dose

Disadvantages

Inefficient delivery from ventiltory circuit
Slow delivery (inactivation)

Selective bronchial instillation

- Using a conventional tube
- Using a double lumen tube
- Via a fiberbronchoscope

Advantages

Local and selected application
Reduced costs

Disadvantages

Difficult technique

Dosing considerations

- Theoretical lipid monolayer = 2 to 5 mg lipid/kg
- Adult surfactant pool size = 3 to 15 mg lipid/kg body weight
- Children 3 to 8 yrs = twice surfactant phospholipid as older children
  Age-related decrease in phospholipid reflects changes in alveolar size

Suggested dosage of natural surfactant

- 50 - 200 mg/kg body weight

Advantages of:

- Single or repeted bolus instillation
- Selective endobronchial instillation
- Aerosolization

Adverse effects of surfactant

- Transient airway obstruction (hypoxemia and hypotension)
- Risks of pulmonary trauma and haemorrhage from increased tidal volume and compliance
- Changes in cerebral perfusion from rapid redistribution of pulmonary blood flow into cerebral circulation

Role of ventilatory support

- CPPV
- HFOV
- ILV
- PEEP

Failure of surfactant therapy to improve lung pathology

- Insufficient dose
- Delayed administration
- Poor distribution
- Excessive inhibition
- Catabolism
- Dilution or lack of endogenous synthesis of the complex

Failure of surfactant therapy to improve lung pathology

- Type of insult
- Degree of the lung injury at the time of therapy
- Complexity of the disease and presence of multiorgan failure (MOF)

Proposed therapy based on lung injury stage at the time of treatment

<u>Characteristics of early stage lung pathology</u>

Uniform lung injury
Not significative reduction of lung compliance

Possibility to use low dosage of surfactant

Aim: prevention of progressive lung disfunction

Therapeutical effect: easier and rapid resolution of lung pathology

<u>Characteristics of late stage lung pathology</u>

Not uniform lung injury
Significative reduction of lung compliance

Increased protein presence in the alveolar spaces

Need to use large dosage of surfactant

Aim: improves physiological parameters
prevention of progressive lung disfunction
allows the lung to heal

Therapeutical effect: difficult resolution of lung pathology

Clinical trials and pilot studies on exogenous surfactant supplementation

1 Neonatal Respiratory Distress Syndrome (RDS)

2 Neonates with lung injury not related to prematurity
- Congenital diaphragmatic hernia
- Meconium Aspiration syndrome
- Bacterial pneumonia

3 Bronchiolitis

4 ARDS
- Sepsis - induced
- Trauma
- Hypoxemic respiratory failure
- Oncohematologic children and adolescents

Clinical trials and pilot studies on neonates with lung injury not related to prematurity

- Congenital diaphragmatic hernia, before and after surgical repair

- Meconium Aspiration syndrome
  - Bolus instillation
  - BAL with reduced doses of Surfactant
  - BAL with reduced doses of Surfactant + SURFACTANT

- Bacterial pneumonia

Problems remained unsolved
- Dose to use
- Repeated doses (when, how, etc.)
- Administration (time, bolus, etc.)
- Immediate and late immunological implication