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Surfactant in pediatric respiratory failure: experience and future perspectives

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Surfactant

- Use in premature babies suffering from RDS
  - Improvement in survival rates
  - Possibility to treat extreme premature

- Jobe AH, Ikegami M. Surfactant for the treatment of respiratory distress syndrome. Am Rev Respir Dis 1987; 136:1256
- Konishi M, Fujiwara T, et al. Surfactant replacement in neonatal respiratory distress syndrome. Eur J Pediatr 1988;147:20
- Coll Europ Multicenter Study Group. Surfactant replacement therapy for severe neonatal respiratory distress syndrome. Pediatrics 1988;147:683

Surfactant

Bolus administration (same method and dose as used in the premature baby)

- Meconium aspiration syndrome
- Bronchiolitis
- ARDS

Surfactant

Meconium aspiration syndrome

- Bolus administration: contrasting results

- ✓ Findlay RD et al. Surfactant replacement therapy in meconium aspiration syndrome. Pediatrics 1996; 97:48
- ✓ Halliday HL et al. Treatment of meconium aspiration syndrome with porcine surfactant. Eur J Pediatr 1996; 155:1047

Surfactant

Meconium aspiration syndrome

- BAL: positive result in animals and humans

- ✓ Paranka MS et al. Surfactant lavage in a piglet model for MAS. Pediatrics 1996; 97:48
- ✓ Cochrane CG et al. Bronchoalveolar lavage with KL4-surfactant in models of MAS. Pediatr Res 1998; 44:705
- ✓ Lam BC et al. Surfactant lavage for MAS: a pilot study. Pediatrics1999; 103:1014

Surfactant

Bolus administration

- Meconium aspiration syndrome
- Bronchiolitis
- ARDS

Surfactant

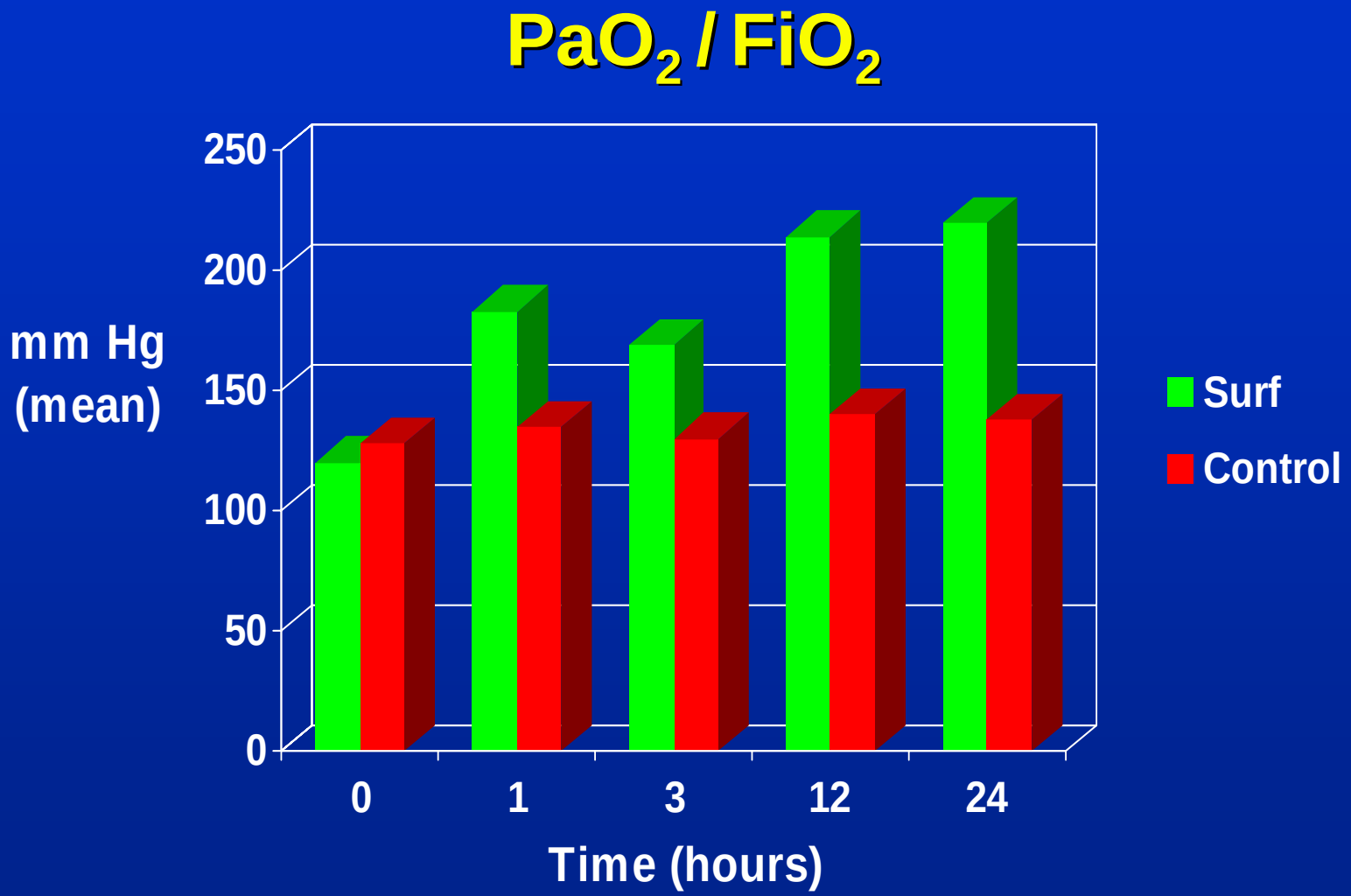
Bronchiolitis

- Therapeutic efficacy from bolus administration (50 mg/kg Curosurf single dose)
- Lung recruitment before treatment and open lung approach after surfactant

❖ Positive effect after 3 hours

- ✓ Luchetti M, Marraro G et al. Porcine-derived surfactant treatment of severe bronchiolitis. Acta Anaesthesiol Scand 1998; 42:805
- ✓ Luchetti M, Marraro G. et al. Multicenter random controlled study of porcine surfactant in severe bronchiolitis. PCCM 2002; 3:261

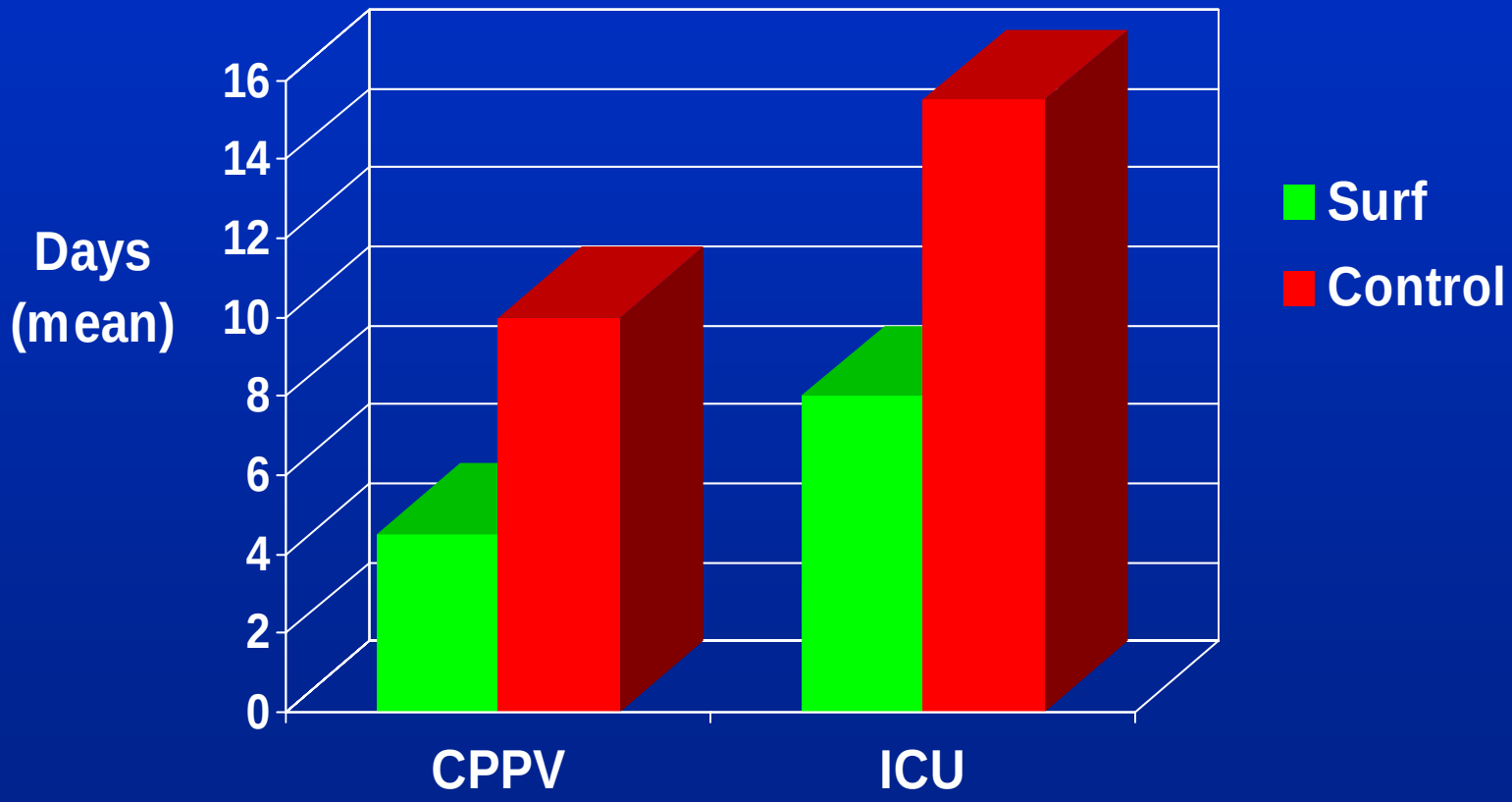
Bronchiolitis



✓ *Luchetti et al. Acta Anaesthesiol Scand 1998*

Bronchiolitis

Duration of intubation and length of PICU stay



✓ *Luchetti et al. Pediatr Crit Care Med 2002*

Surfactant

Bronchiolitis

- Therapeutic efficacy from bolus administration (100mg/kg one or more doses)
- Not recruitment maneuvers before surf

- Positive effects appeared starting from 24 hours

- Tibby SM et al. Exogenous surfactant supplementation in infants with RSV bronchiolitis. Am J Respir Crit Care Med 2000; 162:1251

Use of surfactant

Lesson deriving from MAS

- Need for removal of inhibiting intrapulmonary material (meconium and proteins)

Lesson deriving from bronchiolitis

- Need for lung recruitment and to keep the lung open

Surfactant

Bolus administration (50-800 mg/kg dose)

- Meconium aspiration syndrome
- Bronchiolitis
- ARDS

Surfactant in adults

Acute respiratory failure and ARDS

- Surfactant improves gas exchange but does not impact on survival

- ✓ Spragg RG et al. Chest 1994; 105: 195-202
- ✓ Gregory TJ et al. AJRCCM 1997; 155:1309
- ✓ Spragg RG et al. N Engl J Med 2004; 351:884

Surfactant in pediatric age

ARDS from sepsis (pneumonia) and interstitial pneumonia

- Surfactant improved oxygenation in all patients but decreased mortality only in direct lung pathology

- ✓ Marraro GA et al. Minerva Anesthesiol 1999; 65 (S1):92

Surfactant in pediatric age

ALI in infants, children, and adolescents

- Surfactant acutely improved oxygenation and significantly decreased mortality
- No significant decrease in duration of ventilator therapy, intensive care unit or hospital stay was observed

- ✓ Willson DF et al. JAMA 2005 Jan 26; 293:470

Surfactant in pediatric age

ALI in infants, children, and adolescents

- Willson's study concerns
  - Not stratification of patients for age, not differentiation of lung pathologies

- ✓ Hunt EA et al. Letters. JAMA 2005; 294:898

Surfactant in adults

Lesson deriving from ARDS

Need for

- Treatment of direct lung pathology
- Precocious surfactant application
- Better distribution and local administration

- ✓ Baudouin SV. Exogenous surfactant replacement in ARDS - One day, someday, or never? N Engl J Med 2004; 351:853

Surfactant

Fundamental questions based from existing data

- Could all lung pathology be treated with surfactant?
- Is it necessary to use the same bolus dose used in premature babies?
- Is it necessary recruit the lung and maintain it open?
- Is it possible obtain better result with precocious application?

Fundamental questions based from existing data

Could all lung pathology be treated with surfactant?

Different results according to

- Direct (aspiration, pulmonary contusion, pneumonia) and indirect lung pathology
- Presence of multiorgan failure

- ✓ Spragg RG et al. N Engl J Med 2004; 351:884
- ✓ Marraro GA et al. Minerva Anesthesiol 1999; 65:92

Fundamental questions based from existing data

Is it necessary to use the same bolus dose used in premature babies?

- Need for different surfactant quantity to reduce surface alveolar tension according to age
- Different origin of surfactant deficiency
  - lung immaturity in premature babies
  - surfactant inhibition and inactivation in other ages

Fundamental questions based from existing data

Is it necessary to recruit the lung and maintain it open?

- Need for homogeneity of ventilation by alveolar recruitment before, during and after surfactant

- ✓ Ingimarsson J et al. Acta Anaesthesiol Scand. 2003; 47:968
- ✓ Krause M et al. Am J Respir Crit Care Med 1997; 156:862

Fundamental questions based from existing data

Is it possible obtain better result with precocious application, avoiding compassionate use?

- Precocious treatment is beneficial for survival and outcome

New modalities of surfactant use

When

- Precocious surfactant application

Where

- Direct lung pathology (aspiration, pulmonary contusion, pneumonia)

- How
  - BAL with surfactant diluted in saline
  - Lung recruitment before treatment and maintenance of alveoli and bronchioli continuously open

Surfactant BAL

Advantages

- Removal of material from the lung and reduction in chemical pneumonia, infection and ARDS
- Alveolar recruitment
- Better homogeneity of surfactant distribution

- ✓ Marraro GA. J Mat Fetal Neonat Med 2004; 52:29
- ✓ Balaraman V et al. AJRCCM 1998; 158:12
- ✓ Gommers D et al. Intensive Care Med 1998; 24:494

Disadvantages

- Complex method and need for high skilled staff

BAL and surfactant

- ARDS

- ✓ Wiswell TE et al. Segmental BAL ARDS. Am J Respir Crit Care Med 1999; 160:1188
- ✓ Cochrane GC et al. Surfactant BAL in a model of RDS. Chest 1999; 116:85S
- ✓ Spragg RG et al. Effect of BAL in porcine model of ALI. J Appl Physiol 2000; 88:674
- ✓ Walmrath D et al. Bronchoscopic use in ARDS and septic shock. Eur Respir J 2002; 19:805

Surfactant supplementation

Lung disease with pathophysiology similar to MAS can be treated with surfactant BAL?

Rationale in aspiration and pulmonary contusion

- Direct lung pathology
- Possibility of chemical pneumonia and ARDS development
- Possibility to apply precocious treatment
- Presence of inhibiting and inactivating material that can lead to surfactant deficiency
- Better distribution of surfactant

Surf-BAL in Acute Lung Injury

- Lung contusion from chest trauma in animals

- Strohmaier W et al. Bilateral lavage with diluted surfactant improves lung function after unilateral lung contusion in pigs. Crit Care Med 2005; 33:2286

Surf-BAL in Acute Lung Injury

- Aspiration and lung contusion from chest trauma in humans

- ✓ Vezzol D, Marraro G, et al. Biol Neonate 2002; 81 (S1):99-40
- ✓ Marraro GA et al. Appl Cardiopul Pathophysiol 2004; 13 (S):324
- ✓ Marraro GA. Perspectives for use of surfactant in children and adults. J Mat Fetal Neonat Med 2004; 52:29

Pathophysiology of lung contusion

Characteristics

- Loss of ventilating areas
- Mechanical obstruction of airway by debris, necrotic material, etc.
- Consolidation, necrosis, abscess
- Activation of humoral mediators of inflammation (edema formation)
- Development of infection and ARDS

Surf-BAL in pulmonary contusion

Aims

- Removal of inactivating material present in the lung (blood, necrotic material, markers of acute lung injury, etc.)
- Lung recruitment
- Avoid consolidation of damaged areas
- Avoid secondary injury in the controlateral lung

Pathophysiology of aspiration

Characteristics

- Chemical injury to respiratory epithelium
- Activation of humoral inflammatory mediators (formation of edema)
- Development of chemical pneumonia and ARDS

Surf-BAL in aspiration

Aim of BAL

- Removal of material and inactivating substances from lung
- Prevention of chemical pneumonia and ARDS

- Avoid pathology migration by contiguity of the material

- Lung recruitment
- Stabilization of small airways and alveoli

Surf-BAL in pulmonary contusion and in aspiration

Beneficial effects

- Reduction of intubation and mechanical ventilation duration
- Improvement in gas exchange and pulmonary function

- No complications during and after surfactant-BAL

New perspectives in surfactant supplementation in ALI and ARDS

Need for

- Treatment of direct lung pathology (aspiration, pulmonary contusion, pneumonia)
- Application of protective lung strategy and open and keep the lung open
- Precocius treatment avoiding compassionate use
- Administration of surfactant using a different strategy than bolus

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Thank you for your attention

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