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Original article

# Bronchoalveolar lavage with diluited surfactant in children with severe ARDS

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**Abstract.** Acute respiratory distress syndrome (ARDS) is characterised by damage to the arteriolar-capillary endothelium and alveolar epithelium that leads to surfactant deficiency and atelectasis. Alveolar collapse and pulmonary oedema will further induce surfactant inactivation. Surfactant supplementation has been suggested but the treatment is unpredictable. Poor response may be due to inhibition of administered surfactant by plasma components filling the alveolar space, severity of lung injury, time of surfactant application and inadequate dose. We reported the course of gas exchange and pulmonary mechanics after instillation of surfactant in 14 children (3 months-7 years) with severe ARDS, defined as an OI > 30 and a PaO2/FiO2 <150. We use a diluted concentration of Curosurf (8 mg/ml) divided in 4 aliquots for a total dose of 25 mg/kg. An additional aliquot was use as bronchoalveolar lavage (BAL) before surfactant treatment. All children showed a dramatic response to surfactant with a rapid and progressive increase in compliance and all respiratory mechanics. Mechanical ventilation set was rapidly reduced and gas exchange improved with a PaO2/FiO2 >200 for more than 12 hours. Diluited surfactant lungs lavages were able to increase blood gas exchange in all our patients despite a previous severe gas exchange impairement. (www.actabiomedica.it)

**Key words:** ARDS, pulmonary surfactant, bronchoalveolar lavages, child

## Introduction

Acute respiratory distress syndrome (ARDS) is a lung pathology induced by diverse injuries, including trauma, sepsis, liquid aspiration, inhaled gases, radiation, pneumonitis and many others.

Despite the introduction of new treatments, mortality from ARDS in children remains high (about 40%) (1). ARDS is characterised by damage to the arteriolar-capillary endothelium and alveolar epithelium, including type I and type II pneumocytes (2). Damage to the latter results in surfactant deficiency and atelectasis. Even though surfactant abnormalities in ARDS are not the primary pathogenic factor, surfactant deficiency, either in presence or absence of type II pneumocyte alterations, may result from primary or secondary inhibition or inactivation of pulmonary surfactant in the alveolar space (2, 3). Surfactant deficiency and inactivation will further induce alveolar collapse and pulmonary oedema, leading to the characteristic pathophysiology of ARDS (2, 3).

Surfactant supplementation has been suggested but the outcome is unpredictable (4, 5). Poor response may be due to inhibition of administered surfactant by plasma components filling the alveolar space related to the severity of lung injury. According to this Timing , dosage and modality of surfactant application seem very important (3-5).

In our study we reported gas exchange and pulmonary mechanics in 15 children with severe ARDS treated with repeated brocholaveolar lavages (BAL) of diluited natural porcine surfactant (Curosurf).

## Material and methods

We enrolled all children admitted between January 2005 and December 2007 to the Pediatric Intensive Care Units of A. Gemelli Universitary Hospital and Bambino Gesù Hospital of Rome with severe ARDS defined as an OI > 20 and a PaO2/FiO2 < 150 in patients who require more than 12 cmH2O of mean alveolar pressure under mechanichal ventilation. Children with chronic lung diseases and major cardiac malformations were excluded. This group of children with severe ARDS were treated with broncoalveolar lavage (BAL) using a 10 time diluited concentration of Curosurf (8 mg/ml). Lavage was obtained with an instilled volume of 3 cc/kg of diluted surfactant repeated 3 times for a total surfactant dose of 24 mg/kg. After 5 hand bagging manoeuvres to distribuite well the solution a deep suction of the airways was applied. A corrected procedure was defined when a recovery volume of more than 40% was reached. At the end of this procedure as soon as cardiorespiratory parameters were stabilized we performed a regular instillation of the same diluted surfactant solution used for the lavages through a catheter insert in the endotracheal tube and positioning the infants in 4 classical different decubitus. Suctioning was avoided for the subseguent 2 hours. Gas exchange were monitored continuously by oxygen saturation, end tidal CO2 and trascutaneous monitor (TcCO2 and TcO2). Heart rate, blood pressure, central venous pressure and urine output were also recorded. Monitoring of all cardiorespiratory parameters was continuously performed during the whole procedure and ventilator setting was adjusted to keep SaO2 > 92% and end –tidal CO2 in the range between 40-50 mmHg. Pulmonary function test were performed before, and 30 min, 1 hr ,4 hr, 8 hr, 12 hr, 24 hr, 48 hr and 72 hr after treatment.

## Results

The age of our children ranged between 3 months and 7 years and ARDS had different causes: 1 burn, 1 septic shock, 1 bronchiolites, 1 pulmonary tromboembolism, 1 trauma and 1 pleuropneumonia (Tab. 1). Prism score ranged between 10 e 13 points (Tab. 1). Mechanical ventilation was set in order to reduce baro and volutrauma using small tidal volume, high respiratory rate, permissive hypercapnia and prone position. Two children were under High Frequency Oscillation Ventilation (HFOV). All patients were under corticosteroid treatment.

Every children showed a drammatical response to surfactant with a rapid and progressive increase in compliance from mean 0.43 (range 0.38-0.51) before surfactant treatment to 0.97 (range 0,85-1,2) cmH2O/ml/kg after 12 hour (Fig. 1). Mean OI dropped under 15 (range 5-18) and mean PaO2/FiO2 increased over 250 (range 216-260) in less than 6 hours (Fig. 2). Mechanical ventilation set was rapidly

**Table 1.** General clinical characteristics of studied children

| General clinical characteristic | Age | Gender | Ethiology | PRISM | OI |
|---|---|---|---|---|---|
| 1 | 5 yr | F | Burn | 13 | 36 |
| 2 | 1 yr | F | Sepsis | 12 | 33 |
| 3 | 4mo | M | Bronchiolitis | 10 | 30 |
| 4 | 6mo | M | Pneumonia | 11 | 30 |
| 5 | 2 yr | M | Dic-meningo | 13 | 31 |
| 6 | 6yr | F | Disseminate TBC | 12 | 31 |
| 7 | 3 yr | M | Tonsilectomia | 13 | 32 |
| 8 | 4 yr | M | Ab Ingestis | 13 | 33 |
| 9 | 5mo | M | Bronchiolitis | 10 | 30 |
| 10 | 3mo | F | Bronchiolitis | 11 | 30 |
| 11 | 4 yr | M | Pneumonia | 11 | 31 |
| 12 | 10mo | F | Ab Ingestis | 13 | 34 |
| 13 | 3mo | M | Bronchiolitis | 12 | 32 |
| 14 | 7 yr | F | Trauma | 10 | 30 |

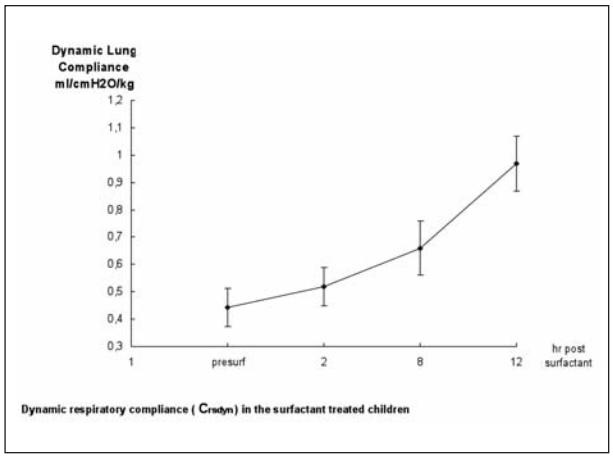


**Figure 1**. Mean ± SD Compliance pre and post treatment in the studied children

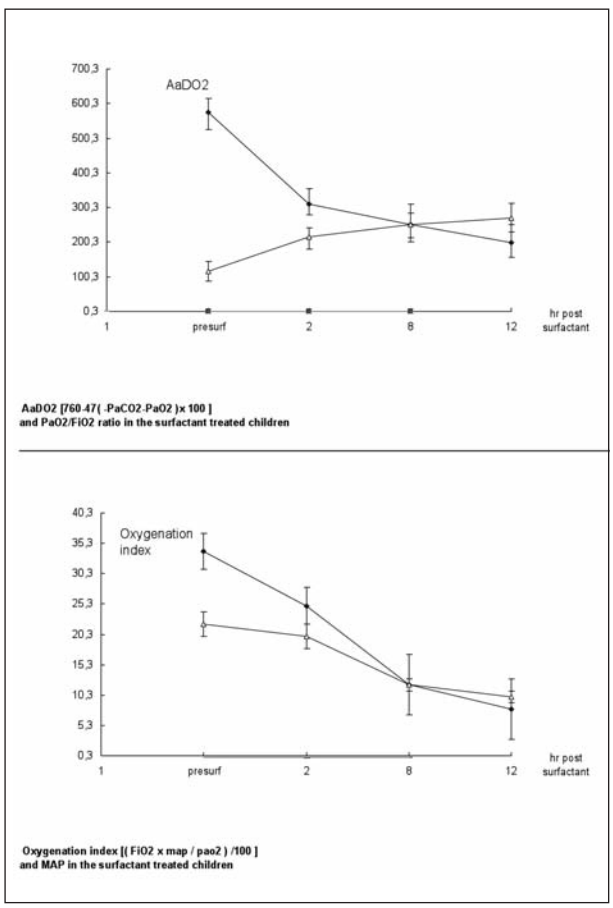


**Figure 2**. Mean ± sd values of Gas exchange in treated children

reduced obtaining a mean MAP < 10 cmH2O and this improvement in gas exchange was kept for more than 12 hours. After that all patients recorded a progressive pulmonary deterioration characterized by an increase in oxygen supplementation. In 6 of 14 children the PaO2/FiO2 ratio returned under 150 and we retreated them with a new dose of diluted surfactant. The response to the second dose was less impressive and more delayed, but in 48 hours all babies increased their PaO2/FiO2 over 250. All patients were extubated and discharged from intensive care unit without major complication. Only 1 babies, which had severe tuberculosis pleuropneumonia, and was under HFOV developed a bilateral pneumothorax and pneumomediastinum in the first hours after surfactant treatment that needed surgical thorax drainage.

## Conclusion

Diluted surfactant lung lavages were able to increase blood gas exchange in all our patients despite all of them suffered severe ARDS with OI > 30. This improvement was faster and more impressive right after the first rather than after the second dose. Many experimental animal data have shown a strong evidence that tracheobronchial lavages with surfactant is extremely efficacious in the most severe forms of ARDS in which alveolar ventilation is extremely eterogenic and the majority of the alveoli are filled with oedema proteins (6-8). When regular instillation of exogenous surfactant is performed its distribution is less homogenise and the small amount of surfactant that reaches alveolar surface is rapidly inactivated by inflammatory and oedema proteins (6-8). This is one of the main reasons why the majority of randomized controlled trials on surfactant treatment in children with ARDS failed to find a benefit effect. A recent meta-analysis reached a statistical significant effect in surfactant treated children in term of reduction of days of mechanical ventilation, days of PICU stay and one study also in mortality (9). Despite the limit of our study that didn't have a control population, it supports very clearly that using lungs lavages with diluited surfactant can improve distribution and efficacy. Larger and randomized control trials should confirm this important finding.

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