CASE REPORT

Exogenous surfactant treatment for severe acute viral bronchiolitis: case report

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Abstract

Objective: to describe the possible clinical and laboratory effects of exogenous surfactant instillation into the tracheal tube of a child with severe acute bronchiolitis undergoing mechanical ventilation.

Case report: a 2-month-old girl with clinical diagnosis of acute viral bronchiolitis underwent mechanical ventilation. She required high positive inspiratory peak pressure (35 to 45 cmH2O) and high inspiratory fraction of oxygen (FiO2 = 0.9), but showed no clinical response or improvement in the arterial blood gas analysis. An exogenous surfactant (Exosurf®, Glaxo - 50 mg/kg) was used to facilitate the use of a less aggressive ventilatory strategy.

Results: four hours after surfactant administration, it was possible to reduce the positive peak inspiratory pressure (PIP) from 35 to 30 cmH2O, and FiO2 from 0.9 to 0.6; and to increase the positive end-expiratory pressure (PEEP) from 6 to 9 cmH2O. During this period the paO2/FiO2 ratio increased from 120 to 266. At the end of 24 hours, FiO2 could be reduced to 0.4.

Discussion: surfactant inactivation may be a decisive factor in the unfavorable evolution of some severe cases of acute bronchiolitis. The tracheal instillation of exogenous surfactant, in these cases, allows us to adopt less aggressive ventilatory strategies, and promotes rapid clinical responses.


Introduction

Surfactants are complex lipoproteins with such a structure that enables them to reduce superficial tension. They are produced by alveolar type II pneumocytes and Clara cells, and their function of maintaining alveolar opening was very well described through hyaline membrane disease models.1 Recent assays have shown the relevance of alveolar opening maintenance and small airway (bronchiole) permeability at the end of expiration, contrasting with the tendency of repetitive collapse and re-expansion of these tubular and elastic structures.2-4

Almost half a century after the findings of Avery and Mead5 about the importance of surfactants for hyaline membrane disease, and after this therapy having become a medical consensus,6 the use of exogenous surfactant in diseases such as the acute respiratory distress syndrome (ARDS), meconium aspiration syndrome (MAS), and bronchiolitis7 has been arousing the interest of researchers.

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Acute viral bronchiolitis is the most frequent pulmonary infection among infants, and is caused by the respiratory syncytial virus in more than 80% of cases. In most cases, acute viral bronchiolitis is benign, and the presence of other morbid states such as prematurity, age below three months, malnutrition, and the presence of cardiopathies predispose a greater probability of hospitalization. 5 to 10% of hospitalized patients are expected to require mechanical ventilation. The therapeutic approaches used in the treatment of acute viral bronchiolitis such as bronchodilators, corticoids, and even ribavirin have yielded conflicting results, and have not reduced morbidity and mortality in a significant way.

Patients with acute viral bronchiolitis presented a reduction in phosphatidylcoline and surfactant protein A, essential components of this complex lipoprotein, causing a significant reduction in its function of maintaining superficial tension when compared to control groups (minimum superficial tension 17 versus 22 mN/m).

Experimental studies conducted on animals with virus-induced pulmonary infection revealed that surfactant restoration drastically changes lung mechanics. A clinical randomized assay involving 20 infants with acute viral bronchiolitis showed that surfactant administration (50mg/kg of Curosurf®, Chiese) improved some oxygenation parameters, reduced PaCO₂, allowed reduction in inspiratory pressure within the first 24 hours, reduced the duration of mechanical ventilation, and also reduced the stay at intensive care unit.

By reporting this case, the authors aim at describing the possible clinical and laboratory effects of the tracheal instillation of exogenous surfactant on an infant with acute viral bronchiolitis submitted to mechanical ventilation.

Case report

EJR, 2 months old, female, non-Caucasian, from the city of Porto Alegre (Brazil), was admitted to the pediatric ICU of the Hospital São Lucas (PUCRS) with rapid onset and progression (around 24 hours according to her mother) of respiratory insufficiency. On admission, the patient presented a great amount of hyaline secretion in her upper airways, activity of the ala nasi, respiratory frequency between 60 and 80 mpm, with intercostal and subcostal retraction, reduced chest expansion, reduced air intake, diffuse wheezing, and prolonged expiratory time. The patient presented alertness, good pulsation, and heart rate around 160 bpm. The chest x-ray accused diffuse interstitial infiltrate, accentuated lung overinflation with left upper lobe herniation, and atelectatic area in right upper lobe. The clinical and radiological status was compatible with severe acute viral bronchiolitis (later confirmed through positive immunofluorescence for respiratory syncytial virus). Although the patient was receiving oxygen at 50%, the clinical response was not satisfactory, and the case evolved into mechanical ventilation twelve hours after admission, due to fatigue.

During the subsequent 24 hours, under mechanical ventilation (Sechrist IV200), the patient continued to have reduced chest expansion despite her high peak inspiratory pressure (35 cmH₂O), respiratory frequency of 20 mpm, inspiratory time of 0.9 seconds, positive end-expiratory pressure (PEEP) of 3 cmH₂O and an inspired oxygen fraction (FiO₂) of 0.6. The patient was properly sedated, and received continued infusion of fentanyl (0.16 mg/kg/min) and midazolam (8 mg/kg/min). Due to the progressive worsening of pulmonary expansion, and persistence of hypoxemia and hypercapnia, the respiratory parameters were alternately modified without favorable results. A PIP up to 45 cmH₂O; FiO₂ of 0.9 were used with respiratory frequency up to 40 mpm to keep PaO₂ around 60-80 mmHg and PaCO₂ between 40 and 50 mmHg. 24 hours after the initiation of mechanical ventilation, due to the unfavorable responses obtained through ventilatory procedures, we decided for the administration of exogenous surfactant (Exosurf® , Glaxo 50mg/kg) directly into the endotracheal tube in 4 aliquots (2 in the dorsal decubitus and 2 in right and left lateral decubitus positions), in an attempt to adopt a less aggressive ventilatory technique (PIP less than or equal to 30 cmH₂O; FiO₂ less than or equal to 0.6; PEEP ~8 to 10 cmH₂O; RF~20 mpm). Before administering the surfactant, we performed a careful endotracheal aspiration combined with neuromuscular block (pancuronium 1 mg/kg), allowing the reduction of PIP to 35 cmH₂O (mean airway pressure of 18.5 cmH₂O); however, the patient still presented inadequate chest expansion.

There was improved pulmonary ventilation immediately after surfactant administration, especially through chest expansion with self-inflating manual ventilation bag. Before surfactant administration, we only obtained a saturation above 90% by keeping the self-inflating bag safety valve closed (40 cmH₂O). It was possible to keep the self-inflating bag safety valve open and restart mechanical ventilation immediately after surfactant administration, gradually reducing the peak inspiratory pressure (PIP), and inspired oxygen fraction (FiO₂). There was a concomitant increase in the positive end-expiratory pressure (PEEP), aimed at recruiting a larger amount of alveolar units. Initially, at the end of four hours after surfactant instillation, and restart of ventilation, we could observe a more distinguished clinical response as to oxygenation rates (PaO₂/FiO₂ ratio = 266). At the end of 24 hours after surfactant administration, it was possible to keep a PIP of 30 cmH₂O, reduce FiO₂ to 0.4, increase the PEEP to 10 cmH₂O with a respiratory frequency of 36 mpm and inspiratory time of 0.7 seconds. As a result, PaO₂/FiO₂ ratio was 173.
The clinical status was stabilized, and ventilation on subsequent days consisted of a PIP between 26 and 30 cmH₂O, respiratory frequency between 20 and 28 mpm, FiO₂ around 0.4 and PEEP between 7 and 10 cmH₂O. On the fifth day of mechanical ventilation, the patient presented septic shock, significantly decelerating weaning; extubation occurred on the 16th day. However, throughout this period, FiO₂ was always below 0.4, and the PIP around 28 cmH₂O, with excellent chest expansion.

Discussion

The administration of exogenous surfactant to patients with alveolar involvement associated with primary deficiency (Hyaline Membrane Disease of the Newborn) or secondary deficiency of endogenous surfactant (Acute Respiratory Distress Syndrome) promotes increased alveolar stability (preventing alveolar collapse), improves pulmonary complacency, facilitates mechanical ventilation, and definitely influences the prognosis.1,5-7

Table 1 - Evolution of results obtained through arterial blood gas analysis and ventilator parameters before and after surfactant administration

<table>
<thead>
<tr>
<th></th>
<th>Presurfactant</th>
<th>1 hour</th>
<th>4 hours</th>
<th>12 hours</th>
<th>24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIP/PEEP/RF/FiO₂</td>
<td>35/640/0.9</td>
<td>33/640/0.6</td>
<td>30/933/0.6</td>
<td>30/835/0.55</td>
<td>30/1036/0.4</td>
</tr>
<tr>
<td>PH</td>
<td>7.24</td>
<td>7.31</td>
<td>7.38</td>
<td>7.23</td>
<td>7.31</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>43</td>
<td>38</td>
<td>35</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>PaO₂</td>
<td>108</td>
<td>76</td>
<td>165</td>
<td>79</td>
<td>78</td>
</tr>
<tr>
<td>Sat O₂</td>
<td>97%</td>
<td>94%</td>
<td>99%</td>
<td>92%</td>
<td>94%</td>
</tr>
<tr>
<td>MAP</td>
<td>18.5</td>
<td>18</td>
<td>18.6</td>
<td>18.3</td>
<td>19</td>
</tr>
<tr>
<td>PaO₂/FiO₂</td>
<td>120</td>
<td>126</td>
<td>266</td>
<td>143</td>
<td>173</td>
</tr>
</tbody>
</table>

Caption: PIP: positive inspiratory pressure; PEEP: positive end-expiratory pressure; RF: respiratory frequency; FiO₂: inspired oxygen fraction; MAP: mean airway pressure
However, in cases where there is a predominance of small airway involvement (meconium aspiration syndrome and bronchiolitis), surfactant administration is still controversial and has not been sufficiently proved\(^3\)\(^,\)\(^4\)\(^,\)\(^7\)\(^,\)\(^9\)\(^,\)\(^15\)\(^-\)\(^18\).

In most situations, the expiratory phase is passive, either in patients with spontaneous or mechanical ventilation. In other words, respiratory musculature is relaxed, and there is reduction in pulmonary volume with exhalation of intralveolar air through the action of elastic retraction, thus allowing for a negative pleural pressure\(^1\)\(^-\)\(^3\)\(^,\)\(^7\) As the lung retracts, bronchiole light is reduced in a way that the terminal airway is blocked at the end of expiration, thus maintaining the residual intrapulmonary volume. At the time of alveolar emptying (exhalation), part of the alveolar surfactant is directed to bronchioles, and, in the bronchiole light, this surfactant will play an important role in reducing superficial tension due to the opening of these airways at the beginning of inspiration\(^1\)\(^,\)\(^2\)\(^,\)\(^4\)\(^,\)\(^7\)\(^,\)\(^9\).

On the other hand, when terminal airways present inflammation (bronchiolitis), expiration becomes active (forced) in an attempt to fight resistance (obstruction) and allow exhalation of trapped intralveolar air. Active expiration occurs through abdominal and thoracic musculature contraction, causing pleural pressure to become positive, carrying it to the terminal airways, resulting in early airway closure and in air trapping\(^1\)\(^,\)\(^2\)\(^,\)\(^4\)\(^,\)\(^7\)\(^,\)\(^9\). Early airway closure keeps most part of the surfactant within the alveoli, preventing it from spreading into bronchioles at the end of expiration, in addition to causing incomplete emptying of the alveoli. Based on this fact, we suppose that local inflammatory process favors its inactivity, reduces its turnover, and its half life as well. Therefore, the bronchioles that collapsed previously will have an increased superficial tension as a result of local surfactant deficiency and of the inflammatory process, which will hinder their opening at the beginning of inspiration. This can explain the high inspiratory pressures that are necessary when these patients are submitted to mechanical ventilation. The subsequent closure and opening of terminal airways lead to an increased consumption of surfactant, enhanced pulmonary resistance, reduced complacency, and induce the release of local inflammatory mediators, contributing to maintain their obstruction\(^1\)\(^-\)\(^3\)\(^,\)\(^9\)\(^,\)\(^10\)\(^,\)\(^19\)\(^,\)\(^21\).

Several studies were conducted to assess the possible application of PEEP so as to prevent terminal airway collapse in patients with small airway obstruction. However, due to process heterogeneity, and high pleural pressure, it was not possible to determine a PEEP value that allowed the recruitment and stability of these airways\(^2\)\(^-\)\(^4\)\(^,\)\(^16\)\(^,\)\(^17\)\(^,\)\(^22\). In healthy postanesthesia patients, an inspiratory pressure around 40 cmH\(_2\)O was estimated in order to allow the opening of atelectatic areas\(^23\).

In view of these facts, we believe patients with severe bronchiolitis submitted to mechanical ventilation will only have their bronchioles reopened (recruitment) through the use of high peak inspiratory pressures. Likewise, we believe that, in order to maintain the patency of these recruited terminal airways, a joint action involving exogenous surfactant administration and progressively higher PEEP is required\(^1\)\(^-\)\(^4\)\(^,\)\(^22\). Among other advantages, these procedures allow the use of lower peak inspiratory pressures for airway reopening at every respiratory cycle, reduced air trapping, improved complacency, reduced airway resistance, prevention of endogenous surfactant destruction and, consequently, minimized side effects caused by mechanical ventilation (reduction in lesions induced by ventilation)\(^19\)\(^-\)\(^21\). Such principles and their potential implications on the clinical evolution of the disease determined the use of a set of synergistic and complementary measures for patients’ clinical well-being. Therefore, the administration of exogenous surfactant would reduce bronchiole superficial tension, minimizing the occurrence of a collapse during expiration, facilitating the opening of bronchioles (recruiting) during inspiration, in addition to reducing the consumption of endogenous surfactant. Likewise, the use of a high PEEP associated with the administration of exogenous surfactant was aimed at reducing superficial tension of these bronchioles during expiration and keeping them open (“recruited”), thus preventing them from collapsing. Consequently, the necessity for high PIP to ventilate these alveoli that are now patent would progressively be reduced\(^20\)\(^,\)\(^22\)\(^,\)\(^23\).

The administration of exogenous surfactant in our patient favored a significant response to pulmonary complacency and resistance, expressed through the chest expansion obtained from progressively lower inspiratory pressures, in addition to improving the PaO\(_2\) /FiO\(_2\) ratio. Improved complacency and reduced pulmonary resistance became clinically evident within the first hours after surfactant instillation, when the FiO\(_2\) and PIP were significantly reduced. Improved lung mechanics associated with surfactant administration evolved rapidly, becoming constant, as 24 hours after administration, the PIP and FiO\(_2\) values were safe and far below those obtained before surfactant administration. This effect and its consequences have fundamental importance for the reduction of injuries induced by mechanical ventilation with respect to pulmonary barotrauma and consumption of endogenous surfactant\(^19\)\(^-\)\(^21\). The literature on the use of surfactants for the treatment of acute viral bronchiolitis in humans is still restricted\(^2\)\(^-\)\(^4\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^15\)\(^-\)\(^18\). A randomized, double-blind study is the most widely known survey into this subject, and reveals immediate results that resemble the ones obtained through our study\(^18\). In the present case report, we observed an improved PaO\(_2\) /FiO\(_2\) ratio after surfactant
administration. Such a difference was clearly evident after 4 hours and was kept for the following 24 hours. Luchetti et al. observed a significantly improved PaO\textsubscript{2}/FiO\textsubscript{2} ratio within the first hour in comparison to the control groups (27.7+/− 2.2 vs 19.0+/− 1.8 P<0.05); this ratio was more evident at the end of 24 hours (30.8 +/− 2.7 vs 19.4 +/− 1.6 P<0.01).

A remarkable difference involving the cases described in the literature refers to the type of surfactant used. Although the synthetic exogenous surfactant (Exosurf) we used may be associated with a tensioactive function and inferior clinical response in vitro or in animal models; few differences have been found in clinical assays when compared to animal studies. The comparison of results obtained from the use of surfactants in respiratory diseases present some methodological difficulties, regarding not only the origin of the tensioactive substance but also the variability of administration methods, dosage variations, and the evoluntional moment of the disease, among others. Even in the presence of these potential confounding factors associated with all limitations a case report presents, there is no doubt that we comparatively share a common hypothesis, which, in the present situation, produced a favorable clinical response, similar to the evolution of patients in Luchetti’s clinical assay.\textsuperscript{18}

These perspectives emphasize the clinical interest in the subject, and consolidate the necessity for controlled studies that assess the consumption and the role of exogenous surfactant in acute viral bronchiolitis, enabling us to decide on a better and appropriate ventilatory technique.

References

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