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Surfactant therapy in patients with acute respiratory failure: report of two cases

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Introduction

Medical treatment with steroids and other drugs, administered while the patient is mechanically ventilated, has been used to treat patients with acute respiratory failure (ARF) [1]. However, the efficacy of such drugs has not yet been established, and the mortality rate for patients with ARF is still high, 50% or more [1]. Some authors have employed surfactant to treat patients with ARF [2,3]. However, the effectiveness of this treatment in ARF has not yet been established definitively, as it has for infant respiratory distress syndrome (RDS). Some improvement is occasionally seen in chest X-ray films, but changes in oxygenation are not consistent.

To evaluate the therapeutic effectiveness of surfactant, we have employed it to treat severe cases of ARF. Here we report the clinical course and outcome of two patients with ARF treated with surfactant.

Case reports

Case 1

A 62-year-old man was admitted with dyspnea. He had experienced respiratory distress during ordinary activities for a period of about 1 month, and he said that his condition had gradually worsened. On admission, he weighed 45 kg and showed orthopnea; the respiratory rate was 40 breaths min^{-1}. Dry rales were auscultated over both lung fields. Chest X-ray films showed diffuse interstitial shadows in both lungs. Examination of blood gas in room air revealed a pH of 7.562, $PaCO_2$ of 28.4 mmHg, PaO_2 of 28.7 mmHg, and a base excess (BE) of 4.1 $mmol \cdot l^{-1}$, values consistent with severe hypoxemia. Oxygenation did not improve even after the patient was placed on mechanical ventilation (pH 7.435, $PaCO_2$ 38.5 mmHg, PaO_2 114.8 mmHg, BE 1.7 $mmol \cdot l^{-1}$ at F_IO_2 1.0, and positive end-expiratory pressure (PEEP) 10 cmH_2O).

Sputum could be aspirated only in small amounts. The sputum culture test was negative and chest X-ray films taken on the following day revealed denser interstitial shadow. Interstitial pneumonia was suspected and steroid pulse therapy was initiated, with methylprednisolone 1.5 g (30 $mg \cdot kg^{-1}$) t.i.d. being administered for 2 days. On day 4 of hospitalization, oxygenation had improved slightly (pH 7.378, $PaCO_2$ 41.7 mmHg, PaO_2 224.6 mmHg, BE 0.6 $mmol \cdot l^{-1}$ at FiO_2 1.0).

However, chest computed tomography (CT) scan showed high-density shadows over the entire lung fields (Fig. 1). The maximum airway pressure reached 40 cmH_2O with reduced pulmonary compliance.

Treatment with Surfacten® (Surfactant-TA; Tokyo Tanabe, Tokyo, Japan) was initiated on day 5 at 24 $mg \cdot kg^{-1}$. The agent was suspended in 50 ml of saline and infused in 10-ml aliquots into each lobe, using a bronchoscope. During the 1st h after administration, tracheal suction was withheld. On the following day, blood gas data (pH 7.376, $PaCO_2$ 57.5 mmHg, PaO_2 263.2 mmHg, and BE 7.0 $mmol \cdot l^{-1}$ at FiO_2 1.0), indicated only slight improvement of oxygenation, but sputum was more easily aspirated and pulmonary compliance had also improved. On chest CT, the diffuse alveolar infiltrates were markedly less extersive, despite the persistent interstitial fibrosis (Fig. 1). The sputum culture was negative, and pulmonary compliance gradually im-

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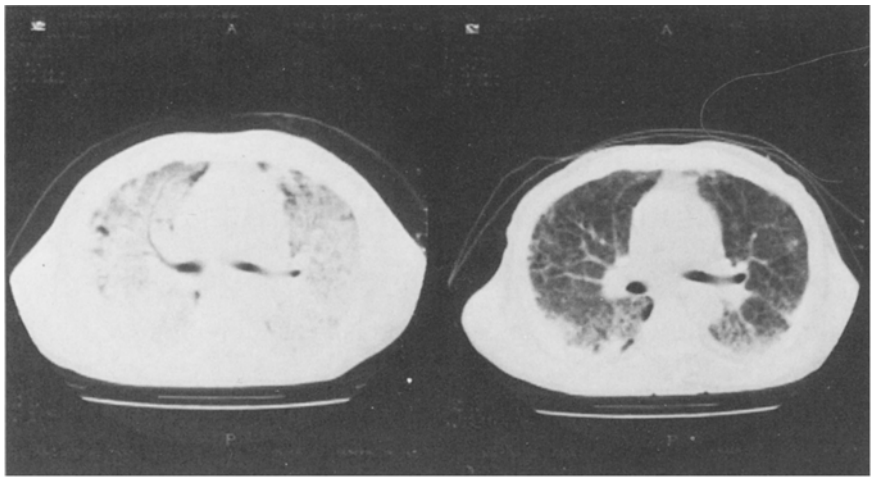

Fig. 1. Chest computed tomography (CT) scan of case 1. *Left*, before the administration of Surfactant-TA; *right*, 24 h after. After the administration of surfactant, the diffuse alveolar infiltrate was markedly reduced, despite the persistent interstitial fibrosis

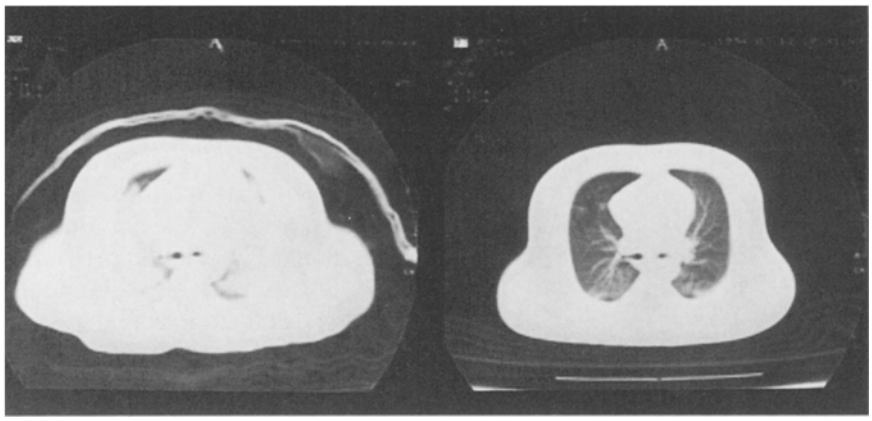

Fig. 2. Chest CT of case 2. *Left*, before the administration of Surfactant-TA; *right*, 8 h after. After the administration of surfactant, marked improvement of the diffuse shadows was observed

proved; the patient was withdrawn from mechanical ventilation on day 8 of hospitalization.

However, 1 day later, the patient's body temperature rose to more than 38°C. Pseudomonas was isolated from the sputum, and oxygenation deteriorated rapidly. The patient died of bacterial pneumonitis on day 18 of hospitalization. At autopsy, interstitial thickening, lymphocyte infiltration of the alveolar septa and interstitium, and fibrosis were observed in the alveolar cavity.

Case 2

A 1-month-old boy was admitted with cyanosis. The patient had been healthy until a few days before admission, when he developed a persistent mild fever and suddenly became cyanotic. The boy had been taken to a nearby hospital and was referred to our hospital with the trachea intubated. On admission, he weighed 4 kg and the respiratory rate was 40 min^{-1}. Cyanosis was noted on the lips. Strong stridor was auscultated and only a small amount of sputum could be aspirated. Chest X-ray films showed diffuse interstitial shadows in both lung fields.

Chest CT also showed diffuse shadows over the entire lung fields (Fig. 2). Blood gas data indicated hypoxemia and respiratory and metabolic acidosis (pH 6.798, $PaCO_2$ 70.4 mmHg, PaO_2 67.2 mmHg, and BE—15.7 $mmol \cdot l^{-1}$ at FiO_2 1.0). Cardiac disorders were ruled out by electrocardiogram (ECG) and echocardiography results. Oxygenation did not improve even after mechanical ventilation was initiated. Despite increased ventilation volume per min, $PaCO_2$ remained between 66 and 80 mmHg and the blood pH between 7.1 and 7.2.

The patient's condition did not improve after a single dose of methylprednisolone (30 $mg \cdot kg^{-1}$), and Surfactant-TA (120 $mg \cdot kg^{-1}$), suspended in 16 ml of saline, was therefore administered via a suction catheter inserted through an endotracheal tube. During the 1st h after administration, tracheal suction was withheld but the respiratory sounds became clearer, and oxygenation and CO_2 excretion improved markedly.

One h after the administration of Surfactant-TA, and thereafter, sputum was readily aspirated. Three h after administration, oxygenation showed dramatic improvement, to 420 mmHg at FiO_2 1.0. Sixteen h after administration, dynamic compliance had increased, and the

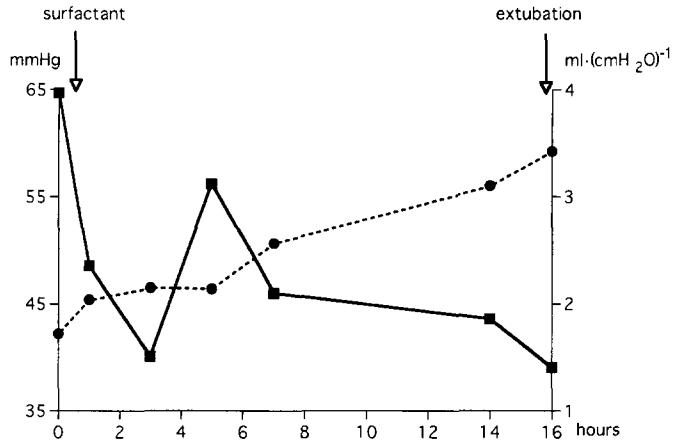

Fig. 3. $PaCO_2$ (*squares*) and pulmonary dynamic compliance (*C-dyn; dots*) of case 2 after Surfactant-TA was administered. After the administration of surfactant, CO_2 excretion was markedly improved and C-dyn increased

patient was extubated without difficulty (Fig. 3). On the following day, marked improvement of diffuse shadows was observed on the chest CT (Fig. 2).

The patient was transferred to the general ward on day 3 of hospitalization, and later the sputum culture was reported as negative.

Discussion

As a result of surfactant therapy, the clearance of sputum was facilitated, pulmonary compliance was improved, and the diffuse infiltrate on the chest CT was markedly diminished in both patients. Improvement of alveolar fluid clearance by surfactant therapy may have contributed to the easier clearance of sputum, as described by De Sanctis et al. [4]. From this perspective, surfactant therapy could be a reasonable and effective choice for ARF.

The major cause of hypoxemia in ARF is the extravasation of plasma protein into the interstitium and alveolar cavities due to the damaged capillary endothelium, leading to interstitial edema that results in fibrosis [1,5,6].

In case 1, the patient's hypoxemia was caused by fibrosis of the interstitium, and the surfactant had negligible effects in improving oxygenation. However, this treatment may help to reduce airway pressure by facilitating the clearance of sputum and it may prevent further damage to the alveolar epithelium [4]. Case 2 however, showed a dramatic improvement after the administration of surfactant. Oxygenation and pulmonary compliance were improved even though tracheal suction was withheld during the 1st h after the administration of surfactant.

It was presumed that fibrosis had not developed in the interstitium in case 2, since he was a newborn and the duration of illness was very short. This may explain the differences between the two patients in the effectiveness of the surfactant. In addition to improving alveolar fluid clearance, surfactant effectively improves gas exchange, decreases airway and alveolar opening pressure, and protects alveolar cells in patients with no interstitial fibrosis [4].

Nosaka and coworkers [3] also administered Surfactant-TA to two patients with ARF, and reported that oxygenation had improved after several doses. They noted that improvement of oxygenation preceded or almost coincided with an improvement in findings on chest X-ray films. In our case 1, despite some radiographic improvement, oxygenation did not increase, whereas in case 2, radiographic signs and oxygenation improved almost simultaneously. As already mentioned, this difference may be related to the underlying pathologies, in particular to the degree of interstitial fibrosis. It has been reported that the effect of surfactant could be enhanced when it is combined with steroids [3]. However, we could not confirm this in our patients.

The optimal dose of surfactant for patients with ARF is another unresolved question. In one study, surfactant (Curosurf [Chiesi Pharmaceuticals, Parma, Italy]), at a dose of $60\,mg \cdot kg^{-1}$, was administered repeatedly to patients with ARF [2]. Approximately 200ml of saline would have been infused intratracheally if we had given the same dose to case 1 as is used for the treatment of RDS. This quantity of fluid seemed to be detrimental to oxygenation, so we used a dose of $24\,mg \cdot kg^{-1}$ for case 1, and a dose of $120\,mg \cdot kg^{-1}$ for case 2 (1-month-old bady), this being equivalent to the dose used for the treatment of RDS. If the purpose of treatment is to facilitate sputum clearance, then repeated small doses of surfactant could be more effective than a single dose [2,7].

There are two methods of administering surfactant in patients with ARF: tracheal instillation and inhalation. However, which of these methods is more effective for the uniform delivery of the surfactant suspension to the damaged regions has not yet been established [8,9]. We administered the surfactant by bolus instillation, since, on the basis of the chest CT findings, we assumed that this method could deliver the surfactant suspension more rapidly and uniformly.

Surfactant therapy showed dramatic improvements in the patient who had no fibrosis in the interstitium of the lung. In the patient with advanced fibrotic changes, however, pulmonary compliance was increased and sputum clearance was facilitated, but arterial oxygenation did not improve.

References

1. Demling RH (1993) Adult respiratory distress syndrome: Current concepts. New Horizons HL1 HL:388–401
2. Richman PS, Spragg RG, Robertson B, Merritt TA, Curstedt T (1989) The adult respiratory failure syndrome: First trials with surfactant replacement. Eur Respir J 2:109s–111s
3. Nosaka S, Sakai T, Yonekura M, Yoshikawa K (1990) Surfactant for adults with respiratory failure. Lancet 336:947–948
4. De Sanctis GT, Tomkiewicz RP, Rubin BK, Church S, King M (1994) Exogenous surfactant enhances mucociliary clearance in the anaesthetized dog. Eur Respir J 7:1619–1621
5. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE (1967) Acute respiratory distress in adults. Lancet II:319–323
6. Petty TL, Silvers GW, Paul GW, Stanford RE (1979) Abnormalities in lung elastic properties and surfactant function in adult respiratory distress syndrome. Chest 75:571–574
7. Merritt TA, Hallman M, Bloom BT, Berry C, Benirschke K, Sahn D, Key T, Edwards D, Jarvenpaa AL, Pohjavuori M, Kankaanpaa K, Kunnas M, Paatero H, Rapola J, Jaaskelainen J (1986) Prophylactic treatment of very premature infants with human surfactant. New Engl J Med 315:785–790
8. Lewis JF, Ikegami M, Jobe AH, Tabor B (1991) Aerosolized surfactant treatment of preterm lambs. J Appl Physiol 70:869–876
9. Zelter M, Escudier BJ, Hoeffel JM, Murray JF (1990) Effects of aerosolized artificial surfactant on repeated oleic acid injury in sheep. Am Rev Respir Dis 141:1014–1019