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Case Report

Treatment of acute respiratory distress syndrome in secondary surfactant deficiency in neonates

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Several studies have shown that the administration of exogenous surfactant is effective in the treatment and prevention of neonatal respiratory distress syndrome (RDS). Nevertheless, premature infants may develop surfactant deficiency. Decrease of surfactant in ARDS might result from many factors, such as inactivation of the surfactant by plasma proteins that enter into the alveolus; inhibition or damage to the protein component or phospholipids component of the surfactant by mediators of inflammation, such as lipases, proteases, or oxidants; incorporation of the surfactant into hyaline membranes; alterations of synthesis, storage, or release of the surfactant as a result of damage to type II pneumocytes , leading to secondary surfactant deficiency (SSD).[1-4]

Normal lung function in infant requires not only adequate surfactant but also adequate airway and alveolar development to support ventilation and gas exchange, the development of chest wall rigidity and diaphragm musculature, and maturation of respiratory control mechanism. In this report we present data of three premature infants who received 1 to 2 doses of surfactant for an acute respiratory deterioration and after initial surfactants treatment for RDS.

Case 1

A baby girl was born at 31 week gestation to a 36 year old primigravida mother by cesarian section for eclampsia. The mother received one dose of steroid before delivering. The birth weight was 1750 g with Apgar scores of 2^{1} and 7^{5}. The diagnosis on admission was RDS and prematurity. Sepsis was ruled out. The infant was admitted to NICU on October 21, 2006. She was placed on conventional ventilation and received two doses of surfactant and antibiotics, in addition to dobutamine. The infant was weaned to nasal oxygen by day of life (DOL) 4 and discharge of nasal oxygen was done by DOL 7. Previous chest X-ray (CXR) did not show diffuse bilateral airspace. CXR done 24 hours showed improved aeration as shown in **Table 1**.

Table 1. Ventilator and saturation parameters pre and post two secondary surfactant doses in case 1

DOL	Time	Type of ventilation	FIO_2 %	PIP	PEEP	Rate Times /min	Saturation %
1	Prior to initial dose	SIMV	100	20	4	56	98
	2 hours after dose	SIMV	70	20	4	56	92
	12 hours after dose	SIMV	70	20	4	56	90
2	Prior to 2nd dose	SIMV	55	20	4	50	94
	1 hour after dose 2	SIMV	40	20	4	35	98
	14 hours after dose 2	SIMV	40	20	4	33	99

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Case 2

A baby girl was born at 26 week gestation to 28 years old primipara mother whose pregnancy was complicated by rupture of membrane (ROM) more than 24 hours prior to emergency cesarean section for fetal distress. The mother received two doses of antenatal steroids. Birth weight was 850 g and Apgar scores were 1^1, 4^5 and 5^{10}. The diagnosis was RDS, suspected sepsis and prematurity. The infant required dobutamine for hypotension in order to prevent renal failure. Chest X-ray did not show diffuse bilateral airspace and pneumonia. CXR done 24 hours later showed no improvement. The infant was admitted to NICU on November 14, 2006. She was placed on conventional ventilation, and received two doses of surfactant and antibiotics for suspected sepsis.

Table 2. Ventilator and saturation parameters pre and post two secondary surfactant doses in case 2

DOL	Time	Type of ventilation	FIO_2 %	PIP	PEEP	Rate Times /min	Saturation %
1	Prior to initial dose	SIMV	100	18	4	60	98
	2 hours after dose	SIMV	80	18	4	60	96
	12 hours after dose	SIMV	70	18	4	60	90
2	Prior to 2nd dose	SIMV	70	18	4	56	96
	1 hour after dose 2	SIMV	80	18	4	50	94
	14 hours after dose 2	SIMV	70	18	4	50	92
	24 hours after dose 2	SIMV	80	18	4	50	92

Case 3

A baby girl was born at 24 week gestation to a 30 year old gravida 2, para 1. The mother suffered from complications of antepartum hemorrhage and had to undergo emergency cesarean section. She received 2 doses of antenatal steroid. Birth weight was 600 g and Apgar scores were 5^1 and 7^5. The diagnosis on admission was RDS and prematurity. Sepsis was ruled out. The baby was admitted to NICU on November 24, 2006. She was placed on conventional ventilation and received two doses of surfactant and antibiotics. The infant required dobutamine for hypotension in order to prevent subsequent renal failure. Chest X-ray did not show diffuse bilateral airspace. CXR done 24 hours later showed no improvement.

Table 3. Ventilator and saturation parameters pre and post two secondary surfactant doses in case 3

DOL	Time	Type of ventilation	FIO_2 %	PIP	PEEP	Rate Times /min	Saturation %
1	Prior to initial dose	SIMV	100	20	4	56	96
	2 hours after dose	SIMV	90	20	4	56	94
	12 hours after dose	SIMV	90	20	4	56	86
2	Prior to 2nd dose	SIMV	100	20	4	50	90
	1 hour after dose 2	SIMV	100	20	4	50	86
	14 hours after dose 2	SIMV	100	20	4	60	60
	24 hours after dose 2	SIMV	100	20	4	60	60

Discussion

Studies have shown that classic, untreated neonatal RDS could develop into worsening condition of pulmonary edema over a few days. Infants are at risk for surfactant dysfunction due to type II alveolar cells injury if they experience respiratory decompensation after a period of days of life from pneumonia/sepsis, pulmonary hemorrhage or aspiration area.[4-10] Moreover, atelectasis, fluid and protein leakage, alveolar inflammation, and release of inflammatory mediators may cause surfactant inhibition and contribute to the development of chronic lung diseases in premature infants. Premature infants with hyaline membrane disease have a deficient quantity of lung surfactant that results in higher alveolar tension and lower compliance properties. This deficiency causes progressive alveolar atelectasis and reduced functional residual capacity. As a result, the affected infants could experience increased effort of breathing, and those with respiratory failure would require mechanical ventilation.[11] Mechanical ventilators pressures and the ensuing volutrauma may cause elastosis and fibrosis at the gas exchanging units and alveolar ducts. The damage seen in the chronic lung disease may not solely be ascribed to the secondary surfactant deficiency or inhibition. Furthermore, administration during secondary insults may markedly improve pulmonary mechanics and help mitigate the inflammatory cascade as seen in Nishina's animal study of acute lung injury due to aspiration. It has also been shown by that study that decreased surface activity can be reversed by raising surfactant concentrations.[12-14]

A number of studies have confirmed a positive response to secondary surfactant administration in infants and children who showed clinical evidence of respiratory failure.[5,6.] Furthermore, other pilot study on 10 infants found surfactant to be effective in reducing oxygen requirements in neonates aged between 9 and 30 days with early chronic lung diseases.[15] Our case series reported good preliminary results of the study.

By comparison, the first case showed positive results, while the second and third ones did not. In this case, we administered two doses of surfactant, but we did not know exactly whether more than two doses would be beneficial to the patient. The appropriate doses was still controversial.[16]

The beneficial effects of surfactant were evident after 24 hours, but not evident after 2 hours, and these effects persisted for the first 7 to 14 days.[17] The birth weight of the first case was 1750 g, while the second and third ones were 600 g and 850 g, respectively. The difference in outcome may be attributed to the fact that the birth weight of the first case was greater than 1250 g. In general, infants with extremely low birth weight (below 1000 g) were at risk of sepsis. Causes of treatment failure included extreme prematurity, preexisting severe hypoxia, hypotension, and acidosis. As the antioxidant system was also immature, the surfactant function could inhibit several proteins leakage. In addition, surfactant could be inactivated by oxygen radicals and enzymes.[16,18- 20]

Further study is needed to evaluate the efficacy of administering surfactant to neonates who experience secondary respiratory failure after recuperation from their initial respiratory distress.

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