Comparison of Outcomes according to the Time of Initial Surfactant Treatment for Very Low Birth Weight Infants: A Multicenter Study

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Purpose: The prophylactic surfactant treatment has been found to improve patient outcomes, compared to the rescue treatment. We performed a multicenter study to determine the relationship between the timing of the initial surfactant treatment and patient outcomes.

Methods: One hundred and seventy one neonates, born at eight different centers, from January 1, 2004 to December 31, 2005, were enrolled. The included subjects were gestational age less than 34 weeks, birth weights less than 1500 g and had respiratory distress syndrome (RDS) that received surfactant. First, a group that received surfactant within two hours after birth was compared to a group that received surfactant after two hours. Next, a group that received surfactant within 30 minutes after birth was compared to a group that received surfactant after 30 minutes.

Results: The mean time after birth at which the initial surfactant was administered to neonates was 140.0 ± 114.3 minutes. The incidence of patent ductus arteriosus (PDA), duration of ventilatory support and hospital days were significantly reduced in the group that received surfactant within two hours after birth. The incidence of PDA and duration of ventilatory support were significantly reduced in the group that received surfactant within 30 minutes after birth.

Conclusion: Surfactant treatment should be provided to premature infants, as soon as possible.

Key Words: Pulmonary surfactant, Very low birth weight infants, Respiratory distress syndrome, Newborn

Respiratory distress syndrome (RDS) is the single most important cause of illnesses and deaths in preterm infants.¹ However, since surfactant replacement therapy has been available as a safe and an effective therapy of immaturity-related surfactant deficiency, since the early 1990s, it has been shown, by careful randomized trials, to reduce the morbidity and mortality of very premature newborns.² Although it has been established that treating RDS with surfactant improves clinical outcomes, many newborns still require mechanical ventilation, which can cause lung injury in preterm infants with RDS, and contribute to the development of chronic lung disease and bronchopulmonary dysplasia (BPD).³ An important question remains concerning the optimal timing of the treatment. There are two basic approaches to the treatment: prophylactic treatment and rescue treatment.³ Prophylactic treatment is defined as the
administration of surfactant through an endotracheal tube, at the time of the initial resuscitation after delivery. Rescue treatment is defined as the administration of surfactant to an intubated baby, several hours after birth and after RDS has been diagnosed.1

Many studies have been performed with regards to the optimal timing of the surfactant treatment and have found that the prophylactic treatment is better than that of the rescue treatment. Yet controversy remains over how to select infants for the prophylactic treatment, and how soon after birth to initiate the therapy. We conducted a multicenter study, at eight centers, to determine the relationship between the timing of the initial surfactant treatment and its associated prognosis.

### Materials and Methods

#### 1. Study centers

This trial was conducted in the neonatal intensive care units of Gangneung Asan Hospital, Kangbuk Samsung Hospital, Konkuk University Medical Center, Konyang University Hospital, Keimyung University Dongsan Medical Center, Dong-A University Medical Center, Sung-Ae Hospital, and Chosun University Hospital in the Republic of Korea. These Hospitals have level 2 and level 3 NICUs that have been established on the national basis, in South Korea. The trial was approved by the institutional review boards of all eight centers.

#### 2. Subjects

One hundred and seventy one neonates who were born in the above eight centers, from January 1, 2004 to December 31, 2005, with birth weights of less than 1,500 g, diagnosed with RDS by clinical and radiographic criteria, and received surfactant treatment were included. RDS was defined as clinical respiratory distress in the presence of chest radiographic evidence of lung field granularity, small lung volumes and air bronchograms as well as fractional inspired concentration of oxygen (FiO2) of 0.4 or more, and a ventilator mean airway pressure of 7.0 cm or more of water, or both. Twenty five neonates, with Apgar scores of 0–3 and who were initially treated with surfactant more than 9 hours after birth, were excluded. One hundred and forty six out of 171 neonates were eligible for the study. All patients received surfactant after diagnosis as RDS. Early rescue therapy is defined as receiving surfactant within 2 hours after birth, and late rescue therapy is defined as receiving surfactant 2 hours later after birth.

Patients diagnosed with RDS received surfactant endotracheally, at a dose of 120 mg/kg. Five aliquots were instilled in each of the following five positions: to the right upper up, the right lower up, the left upper up, the left lower up and the supine. We used Surfacten® (Surfactant, JW pharmaceutical, Mitsubishi Pharma Corporation, Japan)

#### 3. Methods

A retrospective analysis was made of all patients. The information included the time at which the infants received surfactant of the first dose. First, we divided the early and delayed rescue treatment groups on the basis of 2 hours (time that received surfactant after birth), and thereby, compared the variables and outcomes of these groups.2 Next, we divided the early rescue treatment group on the basis of 30 minutes (time that received surfactant after birth), and compared the variables and outcomes of these groups. We compared the survival rate, frequency of pneumothorax, BPD, intraventricular hemorrhage and patent