Complications among Premature Neonates Treated with Beractant and Poractant Alfa

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ABSTRACT

Objective. To compare the complications among preterm infants treated with two different natural surfactants.

Methods. In a randomized clinical trial, 150 preterm infants with Respiratory distress syndrome (RDS) treated with exogenous surfactant, were enrolled in the study. Group A consisted of 79 neonates that received poractant (curosurf). Seventy one newborn infants in group B were treated with beractant (Survanta).

Results. The mean gestational age for group A and B were 29.40±2.90 wk and 29.50±2.73 wk (P=0.82), respectively. The demographic and clinical variables were similar in both groups. The mean duration of intubation (as a primary outcome) was significantly shorter in infants treated with poractant (3.13±1.80 vs 4.06±2.7 days p=0.05). The mean duration of need for oxygen and hospitalization of patients in group A and B were 17.73±22.25 vs 19.14±17.85 days (p=0.67) and 24.89±26.41 vs 29.14±23.54 days (p= 0.32), respectively. There was no significant difference between groups with respect to mortality and morbidity, including pulmonary hemorrhage, intraventricular hemorrhage (IVH), patent ductus arteriosus, sepsis, and bronchopulmonary dysplasia (secondary outcome).

Conclusions. In this study, infants who received poractant had shorter duration of intubation than infants treated with beractant, without any difference in the duration of oxygen therapy or hospitalization. There was no significant superiority of poractant over beractant.

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Key words: Poractant; Respiratory distress syndrome; Beractant; Morbidity

Acute respiratory distress syndrome (RDS) secondary to surfactant deficiency, is a major cause of morbidity in premature infants. Surfactant lines the alveolar surfaces in the lungs, thereby reducing surface tension and preventing atelectasis. Surfactant replacement therapy reduces the severity of RDS and its mortality.¹ ² A wide variety of surfactant preparations have been developed. Animal derived surfactants in clinical use are modified or purified from bovine or porcine lungs and contain proteins.¹ ² Beractant (survanta) are lipid extracts of bovine lung mince, with added dipalmitoyl phosphatidyl choline (DPPC), tripalmitoyl glycerol, and palmitic acid. Poractant (curosurf) is a porcine lung mince that has been subjected to chloroform-methanol extraction and further purified by liquid gel chromatography. It consists of approximately 99% polar lipids (mainly phospholipids ) and 1% hydrophobic low-molecular-weight proteins (SP-B,SP-C).⁴

All commercially available natural surfactants are effective in prevention and treatment of respiratory distress syndrome. There are several studies comparing administration of synthetic surfactants with natural surfactant extracts in the treatment of RDS in preterm infants; that showed greater early improvement in the requirements for ventilator support, fewer air leaks and fewer deaths associated with natural surfactant preparations.¹²⁴ It must be noted that in these studies synthetic preparations did not contain surfactant protein analogues. Many natural surfactant products are available for clinical use. However, it is unclear whether significant differences exist among the available products. There is no current evidence establishing the superiority of one or more natural surfactant products over others. This study was conducted to compare the effectiveness of two animal derived surfactants with different extraction and formulation in the treatment of RDS in preterm infants.
MATERIAL AND METHODS

From March 2008 through March 2009, a prospective masked randomized control trial was conducted in the neonatal intensive care unit of Al-Zahra Hospital, a university level III neonatal centre in North West of Iran. The study was approved by ethics committee of the university. New born preterm infants diagnosed with RDS, that required exogenous surfactant replacement therapy, were eligible for this study. Infants with major congenital malformations, chromosomal abnormalities, and severe asphyxia (5-min Apgar score less than 3), were excluded. They were randomized into two groups by odd or even number of admission code, after obtaining informed parental consents. The group A was treated with poractant alfa (Curosurf, Chiesi farmaceutici, Italy) 200mg/kg (2.5cc/kg) in two divided doses, administrated by rapid bolus infusion directly in to the distal endotracheal tube after disconnecting the infant from ventilator.

The patients in group B was treated with survanta (beractant, Ross, USA) 100 mg/kg (4cc/kg) in four divided doses, intratracheally. Exogenous surfactant replacement therapy was administrated as soon as possible after intubation and stabilization of newborn infant after birth. Primary outcome was that the newborn remained without ventilator support through 7 days of age. Secondary outcomes included death before discharge and complications related to either prematurity or RDS, which included following:

1. Pulmonary hemorrhage, which was diagnosed by a rapid deterioration in clinical condition along with presence of frank blood in the endotracheal tube
2. Bronchopulmonary dyspasia that was defined as oxygen dependency beyond 36 wk post conception age
3. Patent ductus arteriosus (PDA) was defined as confirmation of clinical signs of PDA with echocardiography
4. Air leak syndromes including pneumothorax, and pulmonary interstitial emphysema
5. Retinopathy of prematurity confirmed by ophthalmologic examination performed by same ophthalmologist who was blind to surfactant type received
6. Severe intra ventricular hemorrhage (grade III or IV) that was detected by transfontanel ultrasound evaluation
7. Sepsis documented by positive blood culture

The diagnosis of morbidities was recorded by two independent senior attending neonatologists who did not know the group assignment of the neonates. Infants were eligible to receive additional doses of surfactant, if they met following criteria: requirement for assisted ventilation with Fio2 ≥ 0.50 and radiographic evidence of RDS in presence of continued respiratory distress.

Statistical analysis was performed using the SPSS package 16. The chi-square ($\chi^2$) test was used to analyze the categorical data along with fisher’s exact test when applicable; the student’s t test was used for continuous data.

RESULTS

There were 309 newborn premature infants admitted to NICU during the one year study period. Of these infants, 120 didn’t develop signs and symptoms of RDS and did not receive surfactant; 27 infants had Apgar score less than 3 at 5 min, 12 neonates had major congenital anomalies. A total of 150 infants had met inclusion criteria in the study: 79 in group A and 71 in group B. The mean gestational age and weight of studied infants were 29.45±2.81 wk and 1444.4±585.58 g, respectively. The mean age of infants at the time of surfactant therapy was 7.78±0.75 h. Demographic characteristics did not differ between two groups (Table 1). FiO2 requirement before and one hour after surfactant replacement therapy was not different between two groups (Table 2). Although the mean duration of intubation and need for assisted ventilation was significantly shorter in infants who received curosurf, but the mean duration of hospitalization and O2 therapy were not significantly different between two groups. There were no significant difference in the morality and morbidity among two groups (Table 3). Seventy four (93.7%) patients in group A were treated with one dose and 5 cases (6.3%) needed two doses of curosurf. Sixty seven (94.4%) patients in group B received one dose and 4 cases (5.6%) two doses of survanta.

| Table 1. Demographic Characteristics of Studied Infants |
|-----------------|-----------------|-----------------|-----------------|
| **Group** | **P.Value** | **Male, n (%)** | **Birth weight, gr** | **Gestational age, wk** | **Age of treatment, h** | **Cesarean section, n (%)** |
| A | 45 (57.7) | 1438.7 ± 642.82 | 29.40 ± 2.90 | 6.89 ± 0.85 | 48 (63.2) |
| B | 43 (64.2) | 1450.7 ± 519.01 | 29.50 ± 2.73 | 8.77 ± 1.28 | 50 (70.4) |

* mean ± SD
Group A= Poractant
Group B= Beractant

Maternal treatment with antenatal corticosteroids was completed in 36 (45.5%) cases of curosurf group and 30 (42.3%) cases in survanta group.

DISCUSSION

All regimens of replacement therapy with surfactant...