Comparison efficacy of Curosurf and Survanta in preterm infants with respiratory distress syndrome

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Abstract: This study aim was to compare the therapeutic efficacy of Curosurf and Survanta in preterm infants which were admitted into NICU. In this interventional study, 150 preterm infants divided randomly in two groups (75 in Survanta and 75 in Curosurf). Data analyzed by statistical methods in SPSS.19. The significance level was considered to be P<0.05.There were no statistically significant differences in gestational age, birth weight, mortality rate, pneumothorax, Brunch-Pulmonary Dysplasia (BPD), Intra Ventricular Hemorrhage (IVH) and the mean duration of hospitalization between two groups. But in repeating dose of Survanta group with 67.7% was higher than Curosurf group with 32.3% (p=0.043) and in mean duration of ventilation Survanta group with 8 days was lower than Curosurf group with 10.5 days (P=0.001). Results showed in treatment of RDS in preterm infants each of two groups had similar side-effects but the need for repeated doses in Curosurf group and need for ventilation in Survanta group is less than others .

Keywords: Preterm infants, respiratory distress syndrome, surfactant, efficacy.

INTRODUCTION

Respiratory distress syndrome (RDS) is observed in prematurely born infants and as a common cause of morbidity and mortality in preterm infants; a defect in the development of the lung is usually seen in preterm birth and occurs due to lack of surfactant (Ma *et al*., 2012).

Respiratory distress syndrome deal to mortality in preterm infants; thus, surfactant replacement of surfactant has been the only effective and important treatment for Respiratory distress syndrome and has decreased the pneumothorax and mortality rates of preterm infants with Respiratory distress syndrome. Recently the effectiveness of surfactants has been performed by many studies and meta-analyses (Jeon *et al*., 2015).

Pulmonary surfactant deficiency leads to extensive atelectasis, the disappearance of the remaining lung capacity and disorient the ratio of ventilation for perfusion. The consequences of this state, is weakness of the respiratory muscles and decreased pulmonary compliance which associated with reduced oxygenation, cyanosis, respiratory and metabolic acidosis and with increased pulmonary vascular resistance and right to left shunt through the duct lead to more hypoxemia (Engle *et al*., 2008; Shahfarhat *et al*., 2006).

Some studies showed that preterm infants before 32 gestational age have structurally immature lungs at the secular stage of development and the surface area and diffusion distance for gas exchange are not normal (Fujiwara *et al*., 1980; Halliday *et al*., 2005).

The surfactant replacement was firstly reported by Fujiwara, *et al* and then many subsequent trials have been performed with other types of natural surfactants contain foreign proteins that may be potentially immunogenic and infectious (Fujiwara *et al*., 1980; Obladen *et al*., 2005; Moya *et al*., 2009).

This syndrome occurs in 60-80 % of infants with lower 28 week, 15-30% in 32-36 week and 5% in upper than 36 week. The disease despite treatments, maintenance and support measures the causes of 50 percent of all deaths in the neonatal period. In recent years, various types of surfactant administration, as lifesaving treatment or prevention of mortality in these patients has opened a window of hope (Shahfarhat *et al*., 2006).

There are three commonly researched natural surfactants and many RCT studies in the world showed that surfactant replacement therapy has an important role in the prevention or treatment of RDS (Soll *et al*., 2009; Cummings *et al*., 1992; Logan *et al*., 2009; Egberts *et al*., 1993; Zola *et al*., 1993; Onrust *et al*., 1999).

Surfactants are generally reduced mortality from RDS, especially if combined with administration of antenatal corticosteroids (Khalessi *et al*., 2006).

Short-term effects of surfactant administration, including improved oxygen gradient of alveolar - arterial, lower mean airway pressure (MAP), reducing the need for ventilation, increased lung compliance, reduce the incidence of pneumothorax and improvement pulmonary symptoms in the Chest x-ray (Engle *et al*., 2008; Halliday *et al*., 2005; Behrman *et al*., 2000).

These drugs have side effects such as hypoxia, bradycardia, increasing carbon dioxide partial pressure,

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transient decreasingthe brain activity and cause bleeding in the lungs but they doesn't decrease the Broncho - Pulmunary Dysplasia (BPD) (Behrman *et al*., 2000).

Important role of surfactants in the prevention and treatment of RDS is reducing the surface tension in the alveoli (Khalessi *et al*., 2006).

Baroutis and *et al* in study compared the efficacy of three surfactant and showed that Curusurf due to less duration of artificial respiration, supplemental oxygen and hospital stay were better than others (Proquitte *et al*., 2007).

Ramanathan and *et al* in a study showed that the marked reduction in FiO2 was seen in Curosurf group compare to the Survanta group (Ramanathan *et al*., 2004).

Considering the different types of this medication and complications related to each one, the aim of this study was to compare the effect of two types of surfactant (Survanta and Curosurf) in reducing morbidity and mortality in preterm infants with RDS admitted to the NICU of the Ardabil hospitals in 2010-13.

MATERIALS AND METHODS

This is an interventional study that has been done on preterm infants with gestational age <37 week and has HMD. The infants selected by doctor diagnosis, ABG and Chest x-ray, symptoms and clinical signs and need for the artificial respiration. Of patients fulfilled inclusion criteria, 150 preterm infants selected randomly and after blinding divided in two groups and each one receive one type of surfactant (Curosurfor Survanta). Two groups were matched by Gestational age, type of delivery, sex and birth weight. Infants with meconium aspiration syndrome, congenital anomalies, deadly diseases, metabolic diseases, sepsis or other infections, and babies who underwent resuscitation in the delivery room were excluded from the study. The design of this study was evaluated and approved by the ethical committee of Ardabil University of Medical Science. Necessary information about the side effects such as: BPD (oxygen dependency at 28 days), bleeding into the brain ventricles (IVH), pneumothorax, repeating medication, length of stay in hospital and ventilation time were registered for both group in a checklist. In each group, the required dose (100mg/kg) was administered by injection at the distal tracheal tube and until two hours late the endotracheal suction was not done. During administration time and then, infants were monitored and controlled by Pulse Oximetry, arterial blood gas tests and repeated examinations. Data analyzed by statistical methods in SPSS.19. The significant level was P<0.05.

RESULTS

Of all patients 70 (46.7%) were boy and rest of them were girls. The mean gestational age in boys and girls were 29.74 and 29.58 week; respectively. The mean of ventilation time in boys and girls were 11.77 and 11.65 day; respectively.

Of all infants, 28(18.67%) were died, 14.7% have intraventricular hemorrhage, 16.7% have Pneumothorax and 12% have BDP but the differences between two groups wasn't statistically significant.

Results showed that there wasn't a significant difference in gestational age and birth weight between two groups, so we can say that two groups were matched by gestational age and birth weight. The mean of ventilation time in Surfactant Survanta group significantly lower than Curosurf group (p=0.001). The average of hospitalized time in Surfactant Curosurf group was lower than Survanta group but not statistically significant (table 1).

DISCUSSION

Currently one of standard treatments for sever RDS and requiring ventilators, is Surfactant administration. In Proquitte study in infants' clinic in Berlin hospital, there wasn't significant difference in Fio2, Blood gas, BPD incidence in 28 day, IVH, Pneumothorax, PDA and mortality between two groups. Lower incidence rate of NEC in Survanta group compare with Curosurf was not statistically significant. Also, there was not any significant difference in mortality, side effects due to Survanta and Curosurf such as IVH, BPD and PTX in this study. In our study the rate of mortality in Survanta and Curosurf was 20% and 17.3%; respectively which was similar to other studies and this could represent a qualitative and quantitative improvement of nursing services, closer to standard criteria similar to developed countries (Proquitte *et al*., 2007).

In Ramanathan and *et al* study in South California, the efficacy of two Surfactant (Survanta and Curosurf) for RDS was cheeked and results showed that the mean of Fio2 in Curosurf group was lower than Survanta (P=0.005) and in neonates with gestational age lower than 32 or 36 week the rate of mortality in Curosurf was significantly lower than Survanta group (P=0.034) (Ramanathan *et al*., 2004).

In a retrospective multicenter done by Trembath and *et al* , results showed that there were not any differences in air leak syndromes, BPD, NEC, IVH (grade III or IV), and mortality between two surfactants (Trembath *et al*., 2013). Also, in this study the need for repeated dose in Survanta group was more than Curosurf (P=0.043) and there wasn't any significant difference between mortality and

Table 1: Compare means in two surfactant groups

Variables	Groups	N	Mean (SD)	p-value
Ventilation time	Curosurf	75	10.5(4.9)	0.001
	Survanta	75	8(3.7)	
Hospitalization time	Survanta	75	13(4.8)	0.64
	Curosurf	75	11.6(3.9)	

Table 2: Distribution of repeat dose rate by surfactant type

Repeat dose Surfactant type	Yes		No		p-value
	n	%	N	%	
Curosurf	10	13.3	65	86.7	0.043
Survanta	21	28	54	72	

Surfactant type. Which our study result in this matter was similar to other studies (Baroutis *et al*., 2003; Kamrani *et al*., 2008).

In Clark and *et al* study in Florida, there wasn't any significant differences in mortality rate, side effects, NEC and bleeding into the brain between two Surfactant (Infasurf and Survanta) (Clark *et al*., 2001) which was similar to our study results, because the Surfactant type hasn't significant effect on decreasing mortality rate and side effects and this result confirmed by other studies (Trembath *et al*., 2013;Baroutis *et al*., 2003; Clark *et al*., 2001; Singh *et al*., 2011).Singh and *et al* in a study showed that high dose of Curosurf administration compare to Survanat due to low mortality and need for repeated dose (Singh *et al*., 2011).

Fujii and *et al* in study showed that in Curosurf group the need for repeated dose, low ventilation duration, sooner effect and more survival rate is higher than another group (Fujii *et al*., 2010).

In current study, the need for repeated dose in Survanta group was more than Cursurf (p=0.043) and also, the ventilation time in Survanta group was lower than Curosurf group. (p=0.001) The mean of hospitalization duration in Curosurf group same as Survanta group which was similar to Saeidi and *et al* study but not similar to Kamrani *et al* study (Baroutis *et al*., 2003; Kamrani *et al*., 2008; Saeidi *et al*., 2011).

CONCLUSION

Results showed that using two standard drugs (Survanta and Curosurf) in patients with HMD have similar side-effects. For need to low repeated dose we must use Curosurf and for decreasing ventilation time the Survanta is better.

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