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Original Research Article

Comparison between two natural surfactant poractant alfa and bovine lipid extract in respiratory distress syndrome amongst preterm neonates-a quasi-experimental study

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ABSTRACT

Background: A comparison study of two natural surfactants in preterm babies admitted in neonatal intensive care unit (NICU) and sick newborn care unit (SNCU) of a tertiary care hospital to find out efficacy and consequences.
Methods: A Quasi-experimental study. InSurE technique applied for administering Poractant alfa (CUROSURF) and bovine surfactant (NEOSURF) in two comparison group of preterm neonates with respiratory distress syndrome (RDS) during May 2018 to April 2019. The need of mechanical ventilation, oxygen requirement (FiO_2), duration of oxygen requirement and the consequences were assessed.
Results: The CUROSURF is 6.67% more efficacious than NEOSURF in respect to less requirement of mechanical ventilation. The differences were found between two groups in terms of FiO_2 adjusted (33.49% vs 37.17%) and common side effects respectively but the difference of mean duration of oxygenation (69.8 hrs vs 111.9 hrs) was less and statistically significant in CUROSURF group. Mean duration of hospitalization (9.55 day's vs 14.9 days) also were found to be less and statistically significant.
Conclusions: Treatment with CUROSURF was associated with faster improving oxygenation, less additional doses, and decreased need of mechanical ventilation**.**

Keywords: Quasi-experimental, InSurE, Mechanical ventilation, Oxygen requirement, Natural surfactants

INTRODUCTION

Preterm birth is an important issue in developed as well as developing countries. In India, the preterm delivery rate is 12-13% and in Europe and other developed countries, its rate reported between 5 and 9%.[1] Prematurity is one of the major causes of infant mortality rate that was 34.3% of all infant deaths in 2002.[2] RDS is mainly a problem of prematurity and it is caused by insufficient production of surfactant and structural immaturity of the lungs and/or, very rarely, a genetic problem with the production of surfactant associated proteins. RDS occurs in about 50% of preterm infants who are born at 30 weeks of gestation. The incidence of RDS increases with decreasing gestational age and birth weight.[3]A randomized, multicenter masked comparison trial of Poractant alfa versus Bovine surfactant in the treatment of RDS in preterm Infants showed that treatments with Poractant alfa were associated with faster weaning of supplemental oxygen compared with bovine derived surfactant. CUROSURF is a natural surfactant, prepared from pig lungs. It contains almost exclusively polar lipids in particular phosphatidylcholine (about 60%

of the total phospholipids) and 1% of the specific hydrophobic low molecular weight apoproteins SP-B and SP-C. dipalmitoylphosphatidylcholine (DPPC), palmitic acid, and tripalmitin are added to standardize the composition, and to mimic the surfactant properties of natural lung surfactant.[4]

NEOSURF is a natural surfactant also known as BLES [Bovine lipid extract surfactant] derived from bovine lungs by lavage extraction. It contains numerous DPPC being most abundant. It also includes hydrophobic surfactant associated proteins, SP-B and SP-C, which facilitate dispersion of phospholipids. When administered intratracheally NEOSURF is rapidly absorbed forming an active phospholipids mono layer at air-fluid interface.

Differences in FIO_2 between infants treated with Poractant alfa and those treated with bovine derived surfactant were also larger with earlier treatment. Exposure to oxygen, even for brief periods of time in term newborns, has been shown to result in an increased oxidative stress that lasts for at least a month.[5] The purpose of conducting the study was to find out the efficacy of two exogenous natural surfactants in decreasing the need of duration of oxygen, need of ventilation, and the side effects of both respiratory and gastrointestinal system.

METHODS

This study was conducted from May 2018 to April 2019 in NICU and SNCU of department of paediatrics in a tertiary care hospital, Kolkata. The babies having complaint of RDS with pre-term delivery i.e., Gestational age of neonates between 26 weeks to less than 34 weeks with no history of maternal chorio-amnionitis or other maternal and fetal infections, requiring a fraction of inspired oxygen (FIO_2) >0.30 to maintain oxygen saturation (88% to 92%) by pulse oxymeter irrespective of antenatal steroids, were included. RDS as determined by the attending neonatologist that needs to be treated with exogenous surfactant and mechanical ventilation and CPAP. Apgar score <3 at 10 min, birth asphyxia (cord pH <7.0, Apgar score of <3 or less at 10 minutes of age), major birth defects, malformation syndromes were excluded initially, chromosomal or inherited metabolic disorders and proven presence of immunodeficiency, antenatal exposure of illicit substance (e.g., methamphetamines, cocaine, etc., but not marijuana), and HIV/ other congenital viral, bacterial or fungal infection were also excluded.

Initially 51 neonates less than 34weeks amongst admitted babies in NICU and SNCU fulfilling the inclusion criteria within the said duration of one year were included and divided in two interventional group without standard randomized technique for this study.

Ultimately 40 subjects' data could be included and analysed after losses to follow up. Birth weight, gender, delivery type, APGAR 1st, 5th and 10th minutes were recorded. Gestational age was calculated by using modified Ballard score and compared with maternal history and other clinical screening procedure like modified Down`s scoring and Silverman and Anderson scoring system.

The diagnosis of RDS was based on classic signs (tachypnea, retraction, and grunting); radiological lung findings of reduced air content and a reticulo nodular pattern; an air bronchogram; and a need for FiO_2> 30% to maintain oxygen saturation above 90%.[6] Surfactants were administered using InSurE technique. All infants in CUROSURF group received 200 mg of porcine surfactant/kg bodyweight (2.5 ml/kg), divided in two portions instilled into trachea followed by bag and mask ventilation.[7,8] Retreatment with 100 mg/kg per dose were performed within 24 hours if the babies required FiO_2 of >0.3 to keep SpO_2 to 88 to 92%. The maximum cumulative dose was 400 mg/kg. Bovine surfactant was administered intra tracheally at a dose of 135 mg/kg (5.0 ml/kg). Retreatment with NEOSURF was performed as provided the baby was requiring FiO_2 of >0.3 and was still on the ventilator or not. After surfactant administration the baby was reconnected to the CPAP if previously getting, and FiO_2 and CPAP settings were immediately adjusted according to clinical response to maintain adequate blood gases (PaO_2 of 50-70 mm Hg); ($PaCO_2$ 40-50 mm Hg, pH>7.3) with the lowest possible level of FiO_2 and PEEP. To obtain this goal, FiO_2 was lowered first; subsequent adjustments included reduction of insufflations pressure and inspiration: expiration ratio. A PEEP of 4-5 cm H_2O was maintained during the first hours after surfactant instillation.

In this study 3 outcomes were recorded such a: i) need of mechanical ventilation up to 24 hours of giving surfactant and complete duration of mechanical ventilation during hospital stay ii) requirement of FiO_2 every 6 hourly and iii) total duration of exposure to supplemental oxygen. Both the groups were also compared with respect to the complications and consequences arose within 28 days such as; pulmonary interstitial emphysema (PIE), pneumothorax, patent ductus arteriosus (PDA), intracerebral hemorrhage (ICH grade 3 and 4), pulmonary hemorrhage, BPD (dependence to oxygen at 28th days), necrotizing enterocolitis (NEC), septicaemia, bronchopulmonary dysplasia (BPD), and death. Chest X ray pictures were taken. PIE and pneumothorax were diagnosed according to recent definitions.[9] Sequential echocardiograms and Doppler measurements to assess shunting across the ductus arteriosus were obtained whenever there was any suspicion. Ultrasonographic examinations of the head were performed and ICH was classified according to Papile.[10] Patients were observed for pulmonary hemorrhage, defined as the presence of hemorrhagic fluid in the trachea accompanied by respiratory decompensation requiring increased respiratory support or endotracheal intubation associated

within 60 minutes of the appearance of fluid.[11] The subjects also looked for septicemia, defined as clinical signs of systemic infection and positive blood culture.[12] BPD is defined by accessing oxygen requirement at a postconceptional age of 36 completed weeks or discharge in baby born <32 weeks of gestation and at >28 days but <56 days postconceptional age or discharge. Subjects having life-threatening complications like NEC was diagnosed with the help of modified Bell`s staging criteria. Babies born at <32 weeks of gestation and received prolonged oxygen therapy were screened for retinopathy of prematurity (ROP), which is a vaso-proliferative disorders of retina among preterm infant. The data were entered into the Microsoft excel enterprise 2007 spreadsheet and analyses were done by using IBM SPSS Statistics for Windows, version 22.0. Armonk, NY: IBM Corp. 2013 and CATMaker version 1.2.

RESULTS

In CUROSURF group 12 (30%) neonate belongs to 26 to ≤30 weeks of gestational age and 8 (20%) neonate belongs to >30 to <34 weeks of gestation. In NEOSURF group 9 (22.5%) neonates belongs to 26 to ≤30 weeks of gestation and 11 (27.5) neonates belongs to >30 to <34 weeks of gestation. Only 1 (2.5%) neonate had not received antenatal steroid and all other 39 (97.5%) neonate had received antenatal steroid. The 22 (55%) babies had received complete dose of steroid and other 18 (45%) had not received complete dose of steroid. In CUROSURF group 2 (5%) neonates and 6 (15%) neonates of NEOSURF group had received repeat doses of surfactant. Total 11 (27.5%) neonate had required mechanical ventilation of which 5 (12.5%) neonates belong to CUROSURF group and 6 (15%) neonates belong to NEOSURF group that means CUROSURF is 6.67% more efficacious (17% in terms of relative risk reduction) than NEOSURF in respect to less requirement of mechanical ventilation [CER (Control event rate)= 0.300, EER (Experimental event rate)=0.250, relative risk reduction=17%, absolute risk reduction=0.050] (Table 1).

Mean duration of hospitalization was 9.55 vs 14.9 days between two groups respectively (p<0.05). There were differences of mean FiO_2, 33.49% and 37.17% in CUROSURF and NEOSURF group respectively although not statistically significant (T-1.649, df=38 p>0.05). Mean duration of oxygenation in two groups were significantly different (69.8 hours vs 111.9 hours, T-3.153, df=38 p<0.05) (Table 2).

In NEOSURF treated neonates 1 (2.5 %) was having necrotising enterocolitis (p=0.235). In CUROSURF treated 2 (5%) neonates had patent ductus arteriosus (PDA) (p=0.09). The 1 (2.5%) neonate of CUROSURF treated group had intracranial haemorrhage (ICH). One (2.5%) NEOSURF treated neonate had pneumothorax (p=0.235). Two (5%) neonates of both CUROSURF and NEOSURF treated group had pulmonary hemorrhage (p=1.000). CUROSURF and NEOSURF treated 3 (7.5%), 1 (2.5%) neonate died during hospital stay (p=0.282). None of neonate had developed PIE and BPD. ROP had developed 1 (2.5%) neonate each group treated with both the CUROSURF and NEOSURF (Table 3).

Table 1: Distribution of mechanical ventilation requirement in two surfactant groups, N(n_1+n_2)=40 (20+20).

Items	Mechanical ventilation (%)		Total (%)	Test statistics
	No	Yes		
CUROSURF	15 (37.5)	5 (12.5)	20 (50)	OR=1.29, efficacy= 6.67% X^2=0.125, df=1, p>0.05 (0.723)
NEOSURF	14 (35)	6 (15)	20 (50)	
Total	29 (72.5)	11 (27.5)	40 (100)	

Table 2: Differences in mean duration of oxygenation and mean FiO_2 requirement in two surfactant groups, N(n_1+n_2)=40(20+20).

Groups	Mean duration of oxygen (hours)	SD	Test statistics	Mean FiO_2 (%)	SD	Test statistics
CUROSURF	69.8	7.655	T=-3.153, df=38, p<0.05 (0.003)	33.49	7.655	T=-1.649, df=38, p>0.05 (0.107)
NEOSURF	111.9	6.392		37.17	6.392	

Table 3: Comparison of side effects in both the groups.

Surfactants	BPD	ROP (%)	Pneumothorax	NEC (%)	PDA (%)	Death (%)	IVH grade III/IV (%)
CUROSURF	0	1 (2.5)	0	0	2 (5)	3 (7.5)	1 (2.5)
NEOSURF	0	1 (2.5)	1 (2.5)	1 (2.5)	0	1 (2.5)	0

DISCUSSION

The infant mortality rate had been halved in the last 20 years or so, a drop explained largely by the use of replacement surfactant for premature babies. Morbidity is also reduced. Pneumothorax and other forms of air leak have become a rarity for infants with RDS. Currently available all exogenous surfactants reduce the severity of RDS and also reduce overall mortality among premature infants at risk for RDS.

In present study association of gestational age (26 to ≤30 vs >30 to <34 with mean FiO_2 (37.285 vs 33.052) was nearly statistically significant. There were no statistically significant differences between infants treated with surfactant CUROSURF and NEOSURF in mean FiO_2 (33.49% vs 37.17%). The mean duration of oxygen (69.8 hours vs 111.9 hours) and mean duration of hospitalization (9.55 days vs 14.9 days) was also significantly different. The study of Baroutis et al compared natural bovine surfactant and Poractant alpha where they found that treatment with poractant alpha resulted insignificantly less days for ventilation and supplemental oxygen, and shorter length of hospitalization.[13] This study also showed that CUROSURF treated neonate had needed shorter duration of ventilation and supplemental oxygen, and shorter length of hospitalization. According to Gholami there was no statistically significant differences between infants treated with bovine surfactant and CUROSURF in mean gestational age (30.58 vs 29.00 weeks), birth weight (1388 vs 1330 g). There was no significant difference between groups, or in incidence at 28th day of BPD (40.5% vs 40%), IVH III/IV (3.5% vs 13.3%), pneumothorax (20% vs 20%), PDA (28.3% vs 20%), and death 28% vs. 26.6%).[14] In present study there was no statistically significant differences in side effects. Here 5% of infants randomized to CUROSURF received two doses whereas 15% in the NEOSURF treated group (p=0.114, >0.05). Ramanathan et al compared poractant alpha with beractant (natural bovine surfactant) in a randomized, controlled multicentre trial in the United States. Treatment with poractant alpha was associated with faster improving oxygenation, fewer additional doses, and decreased mortality in preterm infants <32 weeks gestation when compared with beractant. 36% of infants randomized to poractant alpha received two or more doses vs 68% in the beractant treated group (p<0.05). In a meta-analysis of the two studies comparing beractant and poractant alpha, neonatal mortality was significantly lower with poractant alpha though it was raised in CUROSURF treated group in our study although not statistically significant. In this study all died neonates were extremely preterm.

In a recent study comparing these two surfactants, Malloy et al extended the observations of Ramanathan where they increase in oxygenation to persist up to 48 hours after treatment with poractant alpha, and a significantly lower number of additional doses with poractant alpha compared to beractant.[15] In a pharmacoeconomic analysis of Poractant alpha vs Beractant using the data from two randomized studies, Marsh et al showed a 20-53% reduction in cost with CUROSURF vs Survanta (Bovine surfactant). Another study by Mussavi et al stated that no significant differences were observed in most of the clinical variables between the three types of natural surfactant, but in neonates ≤32 weeks, the incidence of pneumothorax was significantly higher in the Alveofact group; in neonates >32 weeks, the incidences of PDA, mean hospital-stay length, and mean mechanical ventilation time were also significantly higher in the same group. It thus appears that CUROSURF and Survanta replacement therapies among premature neonates with RDS perform better than Alveofact replacement therapy.[16] Study by Brown et al showed patients treated with poractant alfa had a shorter length of stay (45.0±30.5 days) than patients treated with beractant (65.1±37.1 days) (p=0.010). Rates of pneumothorax, pulmonary hemorrhage, necrotizing enterocolitis, intraventricular hemorrhage, and mortality did not differ significantly between groups.[17]

In a recent systematic review with biological plausibility and pragmatic meta-analysis of respiratory outcomes amongst porcine vs bovine surfactant therapy for preterm neonates with RDS, sixteen articles were included and 14 in the meta-analysis (1491 neonates) which showed 200 mg/kg poractant-α (a porcine surfactant) was associated with lower BPD/mortality, retreatment and lung haemorrhage.

CONCLUSION

CUROSURF is 6.67% more efficacious than NEOSURF for need of reduce no of mechanical ventilation. CUROSURF use was associated with less duration of oxygenation, less duration of hospitalization and reduced requirement of mean FiO_2. CUROSURF needed less repeat doses of surfactant (5% to 15%) in comparison to NEOSURF. Although the consequences varied in two different groups like; in NEOSURF treated 2.5 % neonates had NEC, CUROSURF treated 5% neonates had PDA, CUROSURF treated neonate 2.5% had ICH, 2.5% neonate had pneumothorax. CUROSURF treated 12.5% and NEOSURF treated 20% neonates had developed septicaemia. 2.5% of both CUROSURF and NEOSURF treated neonates had developed ROP.

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REFERENCES

1. Slattery MM, Morrison JJ. Preterm delivery. Lancet. 2002;360:1489-97.
2. Callaghan WM, MacDorman MF, Rasmussen SA, Qin C, Lackritz EM. The contribution of preterm birth to infant mortality in the United States. Pediatrics. 2006;118:1566-73.
3. Chard T, Soe A, Costeloe K. The risk of neonatal death and respiratory distress syndrome in relation to birth weight of preterm infants. Am J Perinatol. 1997;14:523-26.
4. Liechty EA, Donovan E, Purohit D. Reduction of neonatal mortality after multiple doses of bovine surfactant in low-birth-weight neonates with respiratory distress syndrome. Pediatrics. 1991,88:19-28.
5. Ramanathan R, Rasmussen MR, Gerstmann DR, Finer N, Sekar K. North American Study Group. A randomized, multicenter masked comparison trial of poractant alfa (CUROSURF) versus beractant (survanta) in the treatment of respiratory distress syndrome in preterm infants. Am J Perinatol. 2004;21:109-19.
6. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Plavka R et al. European consensus guidelines on the management of neonatal respiratory distress syndrome in preterm infants-2013 update. Neonatology. 2013,103:353-68.
7. Collaborative European Multicenter Study Group. Surfactant replacement therapy for severe neonatal respiratory distress syndrome: an international randomized clinical trial. Pediatrics. 1988;82:683-91.
8. Speer CP, Robertson B, Curstedt T, Halliday HL, Compagnone D, Gefeller O et al. Randomized European multicenter trial of surfactant replacement therapy for severe neonatal respiratory distress syndrome: single versus multiple doses of CUROSURF. Pediatrics. 1992;89:13-20.
9. Speer CP, Reu BD, Harms K, Herting E, Gefeller O. Neutrophil elastase and acute pulmonary damage in infants with severe respiratory distress syndrome. Pediatrics. 1993;91:794-9.
10. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr. 1978,92:529-34.
11. Kienstra KA. Pulmonary hemorrhage. In: Cloherty JP, Eichenwald EC, Hansen AR, Stark AR. (eds.). Manual of neonatal care. 7th edition. New Delh: Wolters Kluwer (India) Pvt Ltd. 2017;443.
12. Speer CP, Rethwilm M, Gahr M. Elastaseoal proteinaseinhibitor: an early indicator of septicemia and bacterialmeningitis in children. J Pediatr. 1987;111:667-71.
13. Baroutis G, Kaleyias J, Liarou T, Papathoma E, Hatzistamatiou Z, Costalos C. Comparison of three treatment regimens of natural surfactant preparations in neonatal respiratory distress syndrome. Eur J Pediatr. 2003;162(7-8):476-80.
14. Saeidi R, Hamedi A, Javadi A. Comparison of side effect of survanta and CUROSURF in decreasing mortality due to respiratory distress syndrome (RDS) in premature infants admitted in NICU of Ghaem Hospital On 2006-2008. Ir J Neonatol. 2013;4:7-12.
15. Malloy CA, Nicoski P, Muraskas JK. A randomized trial comparing beractant and poractant treatment in neonatal respiratory distress syndrome. Acta Paediatr. 2005;94(6):779-84.
16. Mussavi M, Mirnia K, Asadollahi K. Comparison of the efficacy of three natural surfactants (CUROSURF, Survanta, and Alveofact) in the treatment of respiratory distress syndrome among neonates: a randomized controlled trial. Iran J Pediatr. 2016;26(5):e5743.
17. Brown S, Hurren J, Sartori H. Poractant Alfa Versus Beractant for Neonatal Respiratory Distress Syndrome: A Retrospective Cost Analysis. J Pediatr Pharmacol Ther. 2018;23(5):367-71.

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