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Surfactant Replacement Therapy (SRT) in Respiratory distress syndrome (RDS).

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Abstract

SRT (Surfactant Replacement Therapy) has changed the course of disease and outcome of RDS. We undertook this study to audit outcome of surfactant therapy for RDS in preterms and study complications contributing to morbidity and mortality. This is a prospective observational study of all cases of RDS receiving SRT from October 2009 to July 2011. Overall incidence of RDS was 21% among preterms, varyimg inversely with gestational maturity. Survival was 71.3% among those who received SRT. Sepsis was the most common co- morbidity (43.5%). Downe score ≥6 at intubation (RR 7.25 ;95%CI 2.43-22.42 ;P<0.0001) and sepsis (RR 1.93 ;95%CI 1.09-3.41 ;P=0.022) were significant predictors of mortality. The survival of those given SRT improved with increasing gestational maturity and birth weight. Sepsis is an important complication and its presence, along with a high RDS score at intubation are significant predictors of mortality.

Keywords: Surfactant replacement therapy(SRT), Newborn, Survival, Risk factors, Mortality

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Introduction

Surfactant was the first drug developed exclusively for neonates [1]. Since the time when Fujiwara first published in 1980, the use of a modified bovine surfactant on ten preterms, several studies and meta analysis have conclusively proven the benefit of this therapy on neonatal mortality and morbidity [2-5]. The first case report of use of Survanta in India was from a referral hospital in South India in 1994 [6]. According to the National Neonatal Perinatal Database 2002-2003, Hyaline membrane disease affected 1.2% of total live births and formed 13.5% of total neonatal deaths [7]. There is no comprehensive data from all over the country after that time frame. Isolated reports from individual institutes are available [8]. A large proportion of our population is not able to avail surfactant therapy even though it was included in the WHO Essential Drug List [9]. We have been practicing SRT for RDS for the past ten years. The difficulties faced in the first 4-5 years were manifold. Two main deterrents to optimal use were non affordability by the patient and non availability during emergency hours in the nearby medical stores and pharmaceuticals. The delay in procurement therefore led to use of the drug for late rescue most of the time. However since 2007, this barrier was overcome with the availability of the drug in hospital as part of free supplies. Since then we have been able to use surfactant for early selective rescue. This study was undertaken to audit outcome of surfactant therapy for RDS in preterms and study complications contributing to morbidity and mortality.

Material and Methods

We designed and conducted a prospective observational study of all cases of RDS treated with surfactant during the period from October 2009 to July 2011. We practice early rescue surfactant therapy(within 2 hours of life) for those neonates diagnosed with RDS by Chest X ray and who satisfy one of the following: i) Fail to maintain SpO2 above 87% ; or Pao2 <50 mm Hg with rising FiO2 requirements on bubble CPAP of 7 cm H2O or ii) recurrent apnea warranting intubation or iii) PaCO2>65 mm Hg or iv) Worsening respiratory distress scores. Survanta (Abott laboratories) is instilled endotracheally at 4 ml/kg as four aliquots with manual IPPV in between for 15 to 30 seconds to facilitate surfactant distribution. The neonate is then ventilated with pressure controlled time cycled SIMV. Pre and post surfactant PIP are regulated according to chest rise, air entry and SpO2 by a fellow in neonatology at the bedside. Blood gases are done 30 minutes post surfactant, and thereafter for change in ventilator parameters or as per clinical requirement. All maternal, perinatal and neonatal data were collected and analyzed using SPSS statistical software 13.0. Epical 2000 program

was used to compute relative risk and 95% confidence interval for individual risk factors. P value of <0.05 was taken as significant.

Results

There were 27076 live births during the study period. Preterms constituted 10.2% of these. Overall survival with respect to gestational age among preterms are presented in Table 1.

Due to equipment constraints, although 76 neonates born at <28 weeks gestational maturity required SRT, we were able to instill the same only in 26 babies. Others were managed with CPAP and supportive care. The most common co-morbidity was sepsis (in 43.5%). However shock(6.9%), apnea(4.9%), PDA(3.9%), PPHN(3.9%) , pulmonary hemorrhage(3.9%) NNEC(1.9%) and pneumothorax(1%) also contributed to problems. An analysis of risk factors for mortality revealed sepsis (RR 1.93 ;95%CI 1.09-3.41 ;P=0.022) and Downe score ≥6 at intubation (RR 7.25 ;95%CI 2.43-22.42 ;P<0.0001) to be significant predictors of death.

Table 1. *Survival data based on gestational age*

Gestational Age (weeks)	**Total live births**	**Survivors**	**Percentage**
<28	119	32	26.9
28-30	352	284	80.7
30-34	737	695	94.3
>34	1559	1487	95.38

Five hundred eighty two cases of RDS were diagnosed. Incidence decreased with increasing gestational maturity (Table 2). The outcome of surfactant therapy improved directly with gestational age.

Table 2. *Incidence of RDS and outcome of surfactant therapy*

Gestational Age(weeks)	**Live births** (n)	**RDS n (%)***	**Surfactant given (n)**	**Survive d(%)**
<28	119	76(63.8)	26	16(61.5)
28-30	352	169(48.01)	43	30(69.7)
30-34	737	270(36.6)	23	18(78.2)
>34	1559	67(4.3)	9	8(88.8)

**percentages out of total number of live births of respective gestational age groups*
SRT was instituted in 101 babies during the given period. The mean age of administration of surfactant was 1.28±0.9 hrs.

Discussion

The incidence of RDS is reported to be 6.8-14.1% of preterm live births in our country [7]. In our hospital, it is nearly 21%. This high incidence can be explained by the very low coverage of antenatal steroids and referral of many high risk mothers. Surfactant trials and clinical experience have demonstrated the synergistic effect of antenatal steroids in reducing incidence, severity of RDS, need for surfactant and mortality [10]. The coverage of complete course of recommended antenatal steroids among the patients in our study was only 20.8%. All deserving babies could not be given SRT due to practical problems like non availability of back up ventilator.

Multiple trials from the developed world proved beyond doubt that natural and synthetic surfactants reduced neonatal mortality and pulmonary air leaks. Several trials and reviews of appropriate timing, dose, preparation and route are available [11-17]. Prophylactic SRT is known to reduce mortality and BPD but in more preterm babies (<30 weeks maturity). It has been shown to reduce the combined outcome of bronchopulmonary dysplasia or death (RR: 0.85 ; 95%CI: 0.76–0.95 ; NNT: 24) [13]. It is however costly and more effective where the coverage of antenatal steroids is low. We do not practice prophylactic surfactant replacement because of cost factors. Moreover, many babies improve with CPAP without surfactant therapy. Rescue surfactant treatment within two hours of life results in decrease in neonatal mortality and bronchopulmonary dysplasia [11]. The mean age at which our patients received SRT was 1.28±0.9 hrs. Meta analysis of effectiveness of different preparations has demonstrated superiority of natural surfactants over protein-free synthetic products [17]. Although, Curosurf (porcine lung extract) at higher initial doses of 200 mg/kg is reported to be more effective for rescue than a bovine surfactant at 100 mg/kg [14,15], we use the latter due to availability in the hospital. Newer synthetic surfactant with a protein mimic is being studied and holds promise.

Comparison of morbidity revealed high rates of sepsis (43.5%), nearly double that of a recent Korean experience [18]. Our patients are from low socioeconomic status and receive poor antenatal care. Although our gestational age specific mortality after SRT is comparable to previous Indian reports, it is higher than western reports [8,19]. We face problems of inappropriate nurse: patient ratios and overcrowding.

In conclusion we emphasize that very preterm babies still fail to receive SRT routinely due to practical problems like non availability of ventilator and patented CPAP machines at the crucial time. The survival of those given SRT improved with increasing gestational maturity and birth weight. Sepsis is an important complication and its presence ; along with a high RDS score at intubation are significant predictors of mortality.

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