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Research Article

Role of Surfactant by INSURE Approach in Management of Preterms with Respiratory Distress Syndrome

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Abstract: Surfactant replacement therapy by 'INSURE' is a gentle ventilatory approach in preterms with Respiratory Distress Syndrome (RDS) reducing the mortality and is associated with less adverse sequelae than mechanical ventilation. The objective of the present study is to determine the role of surfactant therapy by INSURE in reducing the mortality of preterms with RDS. 59 preterm babies with RDS were included in the study. 32 were given surfactant. 27 preterm infants who could not afford to purchase surfactant were taken as controls. There is statistically significant difference in mortality between two groups (31.5% vs 63%). The commonest cause of death in study group was sepsis (40%) and in control group was respiratory failure (41%). The mean duration of oxygen therapy, CPAP and mechanical ventilation was much less in the study group than in the control group. This study shows that INSURE is safe and cost effective intervention in reducing the mortality and need for mechanical ventilation in preterm infants with RDS.
Keywords: Respiratory distress syndrome (RDS), nCPAP, Mechanical ventilation, surfactant, INSURE, DOWNE'S score.

INTRODUCTION

Surfactant replacement was established as an effective and safe therapy for preterm infants with established RDS by the early 1990's [1]. Surfactant reduces the mortality from RDS to 50 % and decreases the incidence of complications like air leaks and chronic lung disease (BPD). Surfactant is a complex lipoprotein composed of 6 phospholipids and 4 proteins. It reduces the surface tension in the alveoli, prevents atelectasis and maintains FRC in lungs. Immature lungs of preterm are deficient in surfactant which leads to RDS. There are several strategies of surfactant replacement therapy. Prophylactic surfactant therapy is defined as surfactant administration to infants at high risk of developing RDS for primary purpose of preventing RDS rather than treatment of established RDS. Prophylactic surfactant is given after initial resuscitation but within 10 to 30 minutes after birth. This is in contrast to rescue surfactant strategy in which surfactant is given to preterms with established RDS. Prophylactic surfactant therapy was associated with higher incidence of BPD and death and intraventricular hemorrhage when compared with early stabilization with CPAP and selective surfactant administration [2]. Nasal CPAP started early after birth keeps the lungs open and recruitment of alveoli helps to prevent potentially harmful collapse and reexpansion of terminal airspaces [3]. Early CPAP followed by selective admistration of surfactant by INSURE approach (Intubation, surfactant administration and extubate to a non invasive support) is a more gentle ventilatory approach which improves the survival rates and eliminates the need for continued mechanical ventilation. Mechanical ventilation can however be used to provide additional support in newborns not improving with nasal CPAP and INSURE approach. The present study was designed to determine the role of surfactant therapy by INSURE approach in reducing the mortality of preterms with RDS.

EXPERIMENTAL SECTION

The present study was a hospital based prospective interventional study conducted from January 2010 to August 2011 in the Neonatal intensive care unit of GGH, Kakinada. Newborns less than 34 weeks gestation and birth weight of less than 1800 grams were admitted in NICU. Socio economic status of parents, perinatal details and obstetric history of mother were taken in all cases. Gastric aspirate shake test was done to assess the risk of developing RDS. Downe`s score was used to assess the severity of RDS. A chest X-ray was taken immediately after the onset of symptoms. Grading of RDS was based on radiological findings but chest x ray was not obligatory to give surfactant as we wanted to avoid unnecessary delay in treatment. Vitals were monitored at regular intervals.

Inclusion criteria

Preterm infants of less than 24 hrs of age with a birth weight of 1000-1800 gm, gestational age of 28-34 wk, clinical and or radiological evidence of RDS, negative shake test, Downe`s score of >4 and requiring Fio2 of >0.4 to maintain Spo2 of 87-93 % were enrolled in the study.

Exclusion criteria

Preterm babies who are likely to have respiratory failure due to other causes like congenital heart disease, severe congenital malformations, birth asphyxia and history of PROM were excluded from the study.

A total of 238 preterms of 28-34 weeks of gestation were admitted during the study period. 59 babies who met the inclusion criteria were enrolled in the study and informed consent was taken from the parents of enrolled newborns. Affordability of parents to purchase surfactant decided whether the babies were randomized into study group or control group. 32 preterms randomized into study group were intubated, given surfactant as per standard protocol, extubated and connected to nasal CPAP (INSURE). Any complications during & after the procedure were recorded. 27 preterm babies in the control group were placed on nCPAP or intubated and kept on mechanical ventilator based on requirement. INSURE was considered successful if respiratory distress improved with no retractions, Spo2 >90% on Fio2 <30% and PEEP <5cm of water and the baby could be weaned off from CPAP to oxygen. Preterms with CPAP failure (Spo2 <87% despite Fio2>70% &PEEP >7cm of water, severe retractions with PEEP >7 cm of water, recurrent apnea, severe metabolic acidosis or shock requiring inotropic support) were started on mechanical ventilation. The mortality rate and causes of death in both groups were compared. The factors assessed in the surviving preterm babies were occurrence of complications (air leaks, sepsis, IVH, PDA, pulmonary hemorrhage, NEC, apnea, BPD and ROP), duration of mechanical ventilation, CPAP and 02 therapy and duration of hospitalization. The data was recorded in a pre-designed proforma. The results were tabulated and statistically analysed using SPSS 17.0 version.

RESULTS

Of the total 59 preterms included in the study the characteristics of patients in the treatment and control group showed no significant difference in gender distribution, place of delivery, mode of delivery, antenatal risk factors, mean gestational age and mean birth weight (Table 1). There is statistically significant difference in the mortality rate between the study group and control group (31.5% vs 63%) with a p value of < 0.0196. Mortality rates in preterms with 1000 -1250 grams, 1250 – 1500 grams and 1500 – 1800 grams in study group was 40 %, 28.5% and 0% and in control group was 77%, 69% and 20 % respectively (Table 2). Mortality rate in preterms with gestational age of 28 – 29 weeks, 30 – 31 weeks and 32 – 34 weeks in study group was 42%, 33 % and 0 % and in control group was 75%, 75% and 28% respectively.

Common complications encountered during surfactant administration were transient bradycardia and apnea.

Complications during the course of illness in study group and control group included sepsis (15 % and 22%), NEC (6% and 7%), PDA (3% and11%), air leaks (6% and 11%) and ROP (3% and 0 %).

Table 3 shows the causes of death in 2 groups. Sepsis was the commonest cause of death in study group (40%) where as respiratory failure was the commonest cause of death in control group (41%). Pulmonary hemorrhage was more commonly observed in study group (20%) than in control group (6%).

In surfactant group Downe's score started falling from 2 hrs with steep fall at 6 hrs and maximum response at 24 hrs. In control group there was no improvement in Downe's score in first 24hrs (Fig. 1).

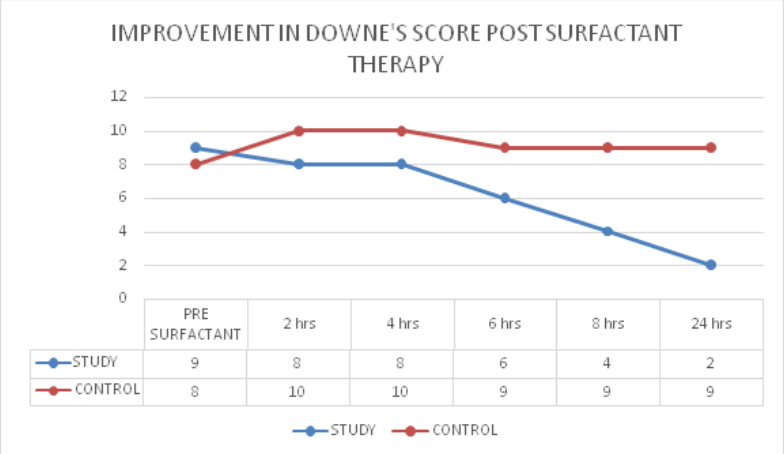

Fig. 1: Improvement in DOWNE'S score post surfactant therapy

Mortality rate was 25%, 33%, 29% and 50% respectively in preterms who were given surfactant at < 6 hrs, 7 – 12 hrs, 13 – 18 hrs and 19 – 24 hrs after birth.

Out of 32 preterms in the study group, INSURE was followed in 24 babies and 8 babies required surfactant followed by mechanical ventilation. 16 babies on INSURE technique were successfully weaned off from CPAP to O2 therapy and discharged. The remaining 8 required reintubation and mechanical ventilation, but only 4 of them survived. Overall survival rate was 83%. Out of 8 babies on mechanical ventilation 6 babies died and remaining 2 babies were weaned from ventilation to CPAP followed by O_2 therapy and discharged. Survival rate in these babies was 25%. In the control group, 15 babies required mechanical ventilation with survival rate of 13%, 12 babies were on nCPAP out of which 9 babies (75%) survived and 2 babies required mechanical ventilation and both died.

The mean duration of CPAP, mechanical ventilation, O_2 therapy and hospitalization was much less in the study group as compared to the control group which was statistically significant with p value <0.0001.

Table 1: Characteristics of patients in the study & control groups

Variable	Study group	Control group
Male babies	17 (54%)	15 (55%)
Female babies	15 (46%)	12 (45%)
Intramural	19 (59%)	13 (48%)
Extramural	13 (41%)	14 (52%)
Vaginal delivery	28 (87%)	22 (81%)
LSCS	4 (13%)	5 (19%)
APH	4	4
Hypertension	5	3
Others	1	3
Birth weight	1200 ± 200 gm	1260 ± 133 gm
Gestational age	30 ± 1.57 wk	30.5 ± 1.46 wk.

Table 2: Mortality in relation to gestational age & birth weight in the 2 groups

	Study group	No. of deaths (%)	Control group	No. of deaths (%)
28-29 wk	14	6 (42%)	8	6 (75%)
30-31 wk	12	4 (33%)	12	9 (75%)
32-34 wk	6	0	7	2 (28%)
1000-1250 gm	20	8 (40%)	9	7 (77.7%)
1251-1500 gm	7	2 (28.5%)	13	9 (69.0%)
1501-1800 gm	5	0	5	1 (20 %)

Table 3: Causes of death in the study & control groups

Cause of death	Study group	Control group
Respiratory failure	3 (30%)	7 (41%)
Sepsis	4 (40%)	5 (29%)
IVH	1 (10%)	2 (12%)
Pulmonary hemorrhage	2 (20%)	1 (06%)
Air leaks	0	2 (12%)

Table 4: Mean duration of ventilation, O_2 therapy & hospitalization in the 2 groups

Variable (No. of days)	Study group	Control group	p value
CPAP	36 hr	68 hr	< .0001
Mechanical ventilation	30 hr	50 hr	< .0001
O2 therapy	96 hr	148 hr	< .0001
Hospital stay	18 days	28 days	< .0001

DISCUSSION

In the present study, a total of 59 preterm babies with RDS were enrolled. Out of these, 32 were given surfactant and 27 who did not get surfactant remained as controls. Demographic variables were uniformly distributed in the 2 groups. The mean gestational age and birth weight of preterm babies in our study were 30 ± 2.81wk and 1200 ± 585.58 gm respectively. In the other studies also the mean gestational age ranged from 29-32 wk and mean birth weight from 1247-1500 gm. The mean age in hours at which surfactant was given was 7.78 ± 0.75 hr in the

present study which was similar to other studies [6, 17]. The mean duration of O_2 therapy in the study group was 4 days which was similar to the observations in Texas [4] & Reininger [5] studies while it was reported 6, 5 & 7 days respectively in other studies [4-7]. The mean duration of mechanical ventilation in the study group was 1.6 days which was correlating with that of Dani *et al*. [7] (1.5 days) and the Texas study (1.4 days) [4]. In other studies [9-13], the duration of mechanical ventilation was comparatively more.

The failure rate of INSURE was 17% in our study compared to 14% & 28% in Ammari *et al*. [13] & Boo *et al*. [14] studies. The most common complication in the study group was sepsis in the present study. Sepsis was reported to be the common complication in other studies also whereas Patent Ductus Arteriosus (PDA) was the most common complication in the studies by Verder *et al*. [6] and others [4, 7, 8, 12]. In the present study, death rate in the study group was 31.5% whereas in the study by Hoekster *et al*. [16], it ranged from 24% to 35%. The most common cause of death in the study group was sepsis which was similar to results observed in other studies done by Corbet *et al*. [17] and Verder *et al*. [6].

The mortality rate in study group was 31.5% and control group was 63%. Respiratory failure was the commonest cause of death in control group. The mean duration of mechanical ventilation, CPAP and oxygen therapy were 20 hrs, 32 hrs and 72 hrs less in surfactant group compared to control group. The mean hospital stay was 10 days less in study group compared to the control group. There is a marked improvement in Downe's score in study group in first 24 hrs. The mortality rate is much less (25%) in preterms who received surfactant at < 6 hrs age showing the importance of early administration of surfactant.

Although surfactant therapy appears very expensive initially, its impact in reducing mortality, duration of ventilation, NICU stay and various morbidities actually decreases the total cost of neonatal care. It also reduces need for mechanical ventilation with all its attendant complications. As surfactant administration is a cost effective intervention, its role is invaluable in those NICUs where resources are limited. Early initiation of CPAP (to keep the alveoli open) with subsequent selective surfactant administration lowers mortality in preterm with RDS. Our study indicates that in INSURE technique, administration of surfactant together with ventilation with CPAP has an add on effect in preventing collapse of alveoli thereby effectively retarding the further progression of RDS in preterm babies. The beneficial effects of INSURE observed in our study are in agreement with the results of other studies where INSURE was employed to manage preterm babies with RDS. Hence INSURE can be recommended as a safe and cost effective modality of respiratory support in preterm babies with RDS especially in resource limited settings.

CONCLUSION

INSURE is safe and cost effective intervention in resourse limited setting which reduces the mortality of preterms with RDS. It reduces not only the need for mechanical ventilation but also the duration of ventilation and period of NICU stay.

Abbreviations used

RDS: Respiratory Distress Syndrome, BPD: Broncho Pulmonary Dysplasia, CPAP: Continuous Positive Airway Pressure, IVH – Intra Ventricular Hemorrhage

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