ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Surfactant Replacement Therapy in Neonatal Respiratory Distress Syndrome: Case Control Study in Rural Hospital, Loni, India.

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ABSTRACT

To determine the role of surfactant in infants with respiratory distress syndrome in rural setup. We retrieved information from the neonates born in our hospital from August 2010 to July 2012 with signs of RDS and gestational age >26wks. Neonates with TTN, Congenital pneumonia and with surgical illness were ruled out. Those infants who received surfactant were taken as Cases and those who did not receive surfactant but managed with only CPAP and ventilator support were taken as Controls. Downe's score (for preterms) and Silverman score (for term neonates) along with chest radiograph was used to assess the severity of RDS and grading was done accordingly. INSURE method was used to instill surfactant followed by nCPAP in Case group and only nCPAP in Control group. Mechanical ventilation (MV) was given in cases requiring it (as per ABG Report). There was significant difference in the outcome of neonates with signs of RDS, who were managed with Surfactant and nCPAP, with or without MV, as compared to those who were managed only with nCPAP, with or without MV but no surfactant. Surfactant administration made a significant difference in the outcome of RDS, with nCPAP. At times MV support was needed but for a shorter duration and lower settings. It is thus recommended that use of surfactant in cases of RDS, particularly moderate to severe cases should become a routine. Respiratory Distress Syndrome, Nasal Continuous Positive Airway Pressure, Mechanical Ventilation.

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ISSN: 0975-8585

INTRODUCTION

Respiratory Distress Syndrome (RDS) was previously referred as Hyaline Membrane Disease (HMD) which occurs after the onset of breathing in newborn due to insufficiency of pulmonary surfactant system. It is characterized clinically by respiratory rate >60/min, dyspnea (intercostal, subcostal in-drawing and sternal retractions) predominantly diaphragmatic breathing pattern and a characteristic expiratory grunt [1]. It is seen primarily in the preterm neonate and is mostly due to pulmonary surfactant deficiency. Lung atelectasis occurs &leads to ventilation perfusion mismatching, hypoxia, and eventual respiratory failure in the untreated infant who has RDS. RDS is diagnosed by physical findings consistent with respiratory distress and characteristic radiographic findings. Treatment of RDS begins antenatally with the administration of maternal steroids to women at risk of preterm delivery between 24 and 34 weeks gestation. It can also occur in term infants, particularly if mother has diabetes. Surfactant (SRT) has been approved for use since 1990 and has been successful in decreasing rates of RDS. Natural surfactant is currently recommended for use, but synthetic surfactant that contains polypeptides to mimic surfactant proteins has shown equally promising results. In general, prophylactic use of surfactant is recommended over rescue treatment in infants at high risk for developing RDS, but the determination of which infants are at high risk for developing RDS remains a clinical one. Early rescue with surfactant administration within two hours is preferred over late rescue but is not always possible in remote & rural areas and economic conditions.The push toward use of less invasive ventilation strategies in the treatment of RDS has led to several trials of nasal continuous positive airway pressure (nCPAP). Results of the SUPPORT trial [2] are pending, but the COIN trial [3] has concluded that nCPAP use in infants who have RDS is not detrimental. Inhaled nitric oxide for RDS still requires investigation on safety and efficacy. Several other treatments have been studied, but as of yet, only inositol administration shows promise in the treatment of RDS. Several complications of the recommended treatments for RDS have been identified, but the benefits far outweigh the risks. Finally, there remains a need for long-term follow-up studies on preterm infants treated for RDS to assess neurodevelopmental outcomes.

In our study the diagnosis and assessment of the severity of Neonatal Respiratory Distress Syndrome clinically and radiologically and management of these neonates with standard treatment modalities will be discussed. The outcome will be assessed with particular emphasis on evaluation of the utility of surfactant administration [4-19.

MATERIALS AND METHODS

This is a prospective study conducted in Neonatal Intensive Care Unit, Rural Medical College (Pravara Institute of Medical Sciences, Deemed University) Loni. Sample size: 150 babies admitted in NICU of Rural Medical College, Loni with the gestational age >26weeks with signs of RDS. Duration of study: July 2010 to July 2012.

Inclusion criteria-

- All neonates with signs of RDS having gestational age >26weeks.

Exclusion criteria-

- Respiratory distress due to other causes, like Transient Tachypnea of Newborn (TTN), Congenital Pneumonia, Pneumothorax and Meconium Aspiration Syndrome.
- Neonates with congenital anomalies.
- Neonates with surgical disorders

In this prospective case control study, cases were enrolled as Control group and Study group. RDS occurs primarily in preterm lungs and surfactant replacement therapy is best approved treatment. The Ethical committee said that since surfactant administration is of proven benefit to preterm with RDS, they should not be deprived of it if agreed to by parents and should form the study group. The Control group should include those neonates whose parents could not afford the surfactant or refused to give consent for its administration after having been explained. All the other monitoring and management modality were common to both the groups. Management modifications were done according to the severity, response and patient individuality.

ISSN: 0975-8585

Thus the Study group consisted of neonates who received surfactant and the Control group consisted of those who did not receive surfactant. Soon after the birth of a neonate, clinical assessment was done. Gestational age was assessed, birth weight, sex, Downe's score/ Silverman's score and chest X-ray was done. According to the severity of the distress appropriate management was started. Humidified oxygen was given by head box or by nasal bubble CPAP. Pulse-oximeter was used to see the oxygen saturation and heart rate monitoring. Chest X-ray was reviewed and clinically co-related. Grading of RDS was done and surfactant was given to consenting parents of the patient. Then the neonates were divided in two groups by above criteria,

1. Neonates were given surfactant intra-tracheally using appropriate sized ET-tube and connector with side-port. Surfactant was administered by INSURE (INtubationSURfactant therapy and Extubation) method, followed by CPAP and some of these cases were given mechanical ventilation if required.
2. The surfactant used in our study was a bovine derived SURVANTA^{TM} (beractant).
3. Dose was 100mg/kg or 4ml/kg.
4. Early Rescue (surfactant given within 2hrs of birth) and late rescue (surfactant given after 2hrs of birth) was given according to severity of baby and affordability of their parents.
5. The CPAP used in our study was conventional Bubble CPAP with humidified oxygen, PEEP and FiO2 control. Minimum pressure was started with 5mm of water and PEEP and Fio2 adjusted according to the need of the patient. Orogastric feeding tube was kept in situ to avoid gaseous gastric dilatation due to CPAP.
6. Ideally minimum of 48hr of CPAP was given to all the preterms with RDS and subsequently weaned off or mechanical ventilation was used according to patient response. Arterial blood gas (ABG) evaluation was done to monitor the need for Mechanical Ventilation.

RESULTS AND DISCUSSION

This prospective study was conducted in our NICU, Rural Medical College, (Pravara Institute Of Medical Sciences, Deemed University) Loni from period of July 2010 to July 2012. It was done to find out the clinical presentations, radiological correlation and the outcome of neonates with Respiratory Distress Syndrome using various modalities of treatment.

The study was done on N=150 cases of Respiratory Distress Syndrome admitted in NICU during July 2010 to July 2012.

The study group received surfactant and the control group did not.

1. In our study the overall incidence of RDS was 1.60%
2. Of the 150 cases, 98(65.33%) were males and 52(34.66%) were females. The incidence of RDS was more in Males as compared to the Females.
3. Out of total 150 cases, vaginal deliveries were 60(40%) and LSCS were 90(60%). Cesarean delivered babies are more prone to develop RDS as compared to the normal vaginal deliveries.
4. Out of 150 cases of RDS, 43(38.66%) neonates were born between 26 to 28weeks, 49(32.66%) neonates were born between 28 to 30weeks, 32(21.33%) neonates were born between 30 to 32 weeks, 17(11.33%) neonates were born between 32 to 34 weeks, 9(6%) neonates were born between 34 to 36 weeks, 2(1.33%) neonates were born >36 weeks.

The incidence of RDS was inversely proportional to their gestational age.

5. Out of 150 cases of RDS, 34(22.66%) neonates were born <1000g, 43(28.66%) neonates were between 1001 to 1500g, 39(26%) neonates were between 1501 to 2000g, 26(17.33%) neonates were between 2001 to 2500g, 8(5.33%) neonates were born >2500g.
6. Out of 150 cases of RDS, 22(14.66%) had **mild RDS,** 76(50.68%) had **moderate RDS** and 52(34.66%) had **severe RDS** clinically. And22(14.66%) neonates had **grade 1**, 34(22.66%) neonates had **grade 2**, 42(14.66%) neonates had **grade 3**, 52(34.67%) neonates had **grade 4**radiologically. Pierson coefficient was 0.7, and it was correlated well.
7. Out of 150 cases, 92(61.32%) babies had received maternal antenatal steroid and out of which 76 (82.60%) babies developed mild to moderate RDS and rest had severe RDS.

Thus maternal antenatal corticosteroids were not fully effective in preventing RDS in preterm but the severity was less and had a more favorable outcome.

8. Early intubation and surfactant replacement therapy followed by extubation to CPAP (INSURE method) showed good results in the form less mortality, compared to the SUPPORT method.
9. The need for positive pressure ventilation in study groups n=58, out of which only 20 (34.50%) babies required MV was less, whereas in the control group n=92, 56 (60.87%) babies required MV were more.
10. The mean CPAP and Ventilatorysettings was less in Study group as compared to the Control group.
11. The duration of oxygen requirement in the study group n=58, was less, Mean SD 2.53±0.94 weeks. Whereas in control group n=92, it was Mean SD 4.48±1.01 weeks.
12. The complications such as PDA and Pulmonary hemorrhage was more in babies who received surfactant and other complications such as BPD and others was more in babies who did not receive surfactant.
13. The duration of hospital stay was less in study group Mean SD 3.53±1.21 weeks and more in control group Mean SD 4.65±1.47 weeks.
14. The mortality of babies according to the gestational age was In 26-28week(n=43), 16(37.20%) survived and 27(62.80%) died, 28-30week(n=49), 32(65.30%) survived and 17(34.70%) died, 30-32week(n=30), 18(60%) survived and 12(40%) died, 32-34week(n=17), 12(70.60%) survived and 5(29.40%) died, 34-36week(n=9) and >36week(n=2) all of them survived(100%). The mortality was inversely proportional to the gestational age. i.e., lesser the gestational age more was the mortality.
15. The mortality of babies according to the Birth weight was; In <1000g(n=34), 16(47.05%) survived and 18(52.94%) died, 1001-1500g(n=43), 12(27.90%) survived and 31(72.10%) died, 1501-2000g(n=39), 28(71.80%) survived and 11(28.20%) died, 2001-2500g(26), 25(96.15%) survived and 1(3.84%) died, in >2500g(n=8) all of them survived(100%). The lower the birth weight more was the mortality.
16. The mortality of babies in study group n=58, was 41(70.68%), and in control group n=92, was 48 (52.17%).The outcome in the form of mortality was more in Control group as compared to the Study group.
17. The mortality of babies according to the timing of surfactant therapy (Early Vs Late Rescue) was; in early rescue group (n=24), 18(76.15%) survived and 6(23.85%) died, in late rescue group (n=34), 23(23.85%) survived and 11(33.45%) died. The early rescue had better outcome and higher chance of survival.

Table 1: Showing study parameters

Parameters	*Case group*	*Control group*
Total no. patients(N=150)	58(38.60%)	92(61.40%)
Number of males(n=98)	42(72.40%)	56(60.86%)
Number of females(n=52)	16(27.60%)	36(39.14%)
Vaginal deliveries(n=60)	22(37.93%)	38(41.30%)
LSCS(n=90)	36(62.06%)	54(58.69%)
Mean duration of CPAP(in wks)	0.5	1.2
Mean duration of MV(in wks)	0.28	0.85
Mean duration of hospitalization (in wks)	3.53±1.21	4.65 ±1.47
Early rescue **Late rescue**	24(41.37%) 34(58.62%)	
Outcome(survived)	41(70.68%)	48(52.17%)

Table 2: Showing complications observed in both the groups.

Complications	Case	Control
IVH	12(20.68%)	19(20.65%)
PH	10(17.24%)	12(13.04%)
PDA	13(22.41%)	8(8.69%)
BPD	08(13.79%)	30(32.60%)
SEPSIS	26(44.82%)	62(67.39%)
PNEUMOTHORAX	2(3.50%)	6(6.52%)

ISSN: 0975-8585

Table 3: Showing comparison of ventilator settings in both the groups.

Ventilatory settings (Mean SD)	*Case group*	*Control group*
PEEP	6.5±0.2	8.4±0.8
PiP	17.5±0.2	20.2±0.6
FiO_2	0.6	0.8

Table 4: Showing the outcome.

Outcome		
Parameters	***Survival***	***Death***
Outcome according to period of gestation		
26-28(n=43)	16(37.20%)	27(62.80%)
28-30(n=49)	32(65.30%)	17(34.70%)
30-32(n=30)	18(60%)	12(40%)
32-34(n=17)	12(70.60%)	5(29.40%)
34-36(n=9)	9(100%)	0
>36(n=2)	2(100%)	0
Outcome according to birth weight		
<1000(n=34)	16(47.05%)	18(52.94%)
1001-1500(n=43)	12(27.90%)	31(72.10%)
1501-2000(n=39)	28(71.80%)	11(28.20%)
2001-2500(n=26)	25(96.15%)	1(3.84%)
>2500(n=8)	8(100%)	0
Early vs Late		
Early Rescue(n=24)	18(76.15%)	6(23.85%)
Late Rescue(n=34)	23(66.55%)	11(33.45%)

CONCLUSION

Surfactant administration made a significant difference in the outcome of RDS, with nCPAP. At times MV support was needed but for a shorter duration and lower settings. It is thus recommended that use of surfactant in cases of RDS, particularly moderate to severe cases should become a routine.

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