

Comparison of Continuous Positive Airway Pressure Therapy with and Without Surfactant in Neonatal Respiratory Distress Syndrome

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Abstract: Neonatal respiratory distress syndrome is an important cause of morbidity and mortality in preterm neonates. Recognition of adverse effects related to mechanical ventilation, led researchers to explore various non-invasive forms of respiratory support. This is a retrospective comparative study done to determine the efficacy of CPAP alone in comparison to that of CPAP with surfactant in the treatment of RDS. The primary objective was determining proportion of babies who could be weaned off without the need for mechanical ventilation. Methods: The study group contained 124 preterm babies between 28 and 32 weeks of gestational age with RDS. Forty two (33.8%) babies were managed on CPAP alone (group A) and 82(66.1%) babies were initially put on CPAP, administered intra tracheal surfactant and were continued on CPAP (group B). CPAP was delivered using the Fisher and Paykel CPAP system. Improvement in respiratory distress and successful weaning off from CPAP were taken as response. All neonatal and CPAP variables, associated complications were analysed. Statistical analysis was performed using the SPSS statistics version 18.0 (SPSS Inc., Chicago, IL, USA). Chi-square test, t-test, and Wilcoxon rank-sum test. The results were considered statistically significant at $P < 0.05$. 26(61.9%) of babies from group A and 64(78%) of babies from group B could be successfully weaned off CPAP. The mean gestational ages, male to female ratio, age at administering CPAP, severity of respiratory distress and F_{iO_2} required at the time of admission were comparable in both the groups. The maximum F_{iO_2} required, the maximum PEEP and the duration of CPAP was significantly higher in group A than in group B. There were eight deaths including two babies who required mechanical ventilation in group A compared to 10 deaths in group B. Group A had higher incidence of pulmonary haemorrhage and pneumothorax. CPAP with surfactant administration is more effective than CPAP alone in neonatal RDS.

Keywords: Preterm, respiratory distress syndrome, CPAP, Surfactant.

INTRODUCTION

Neonatal respiratory distress syndrome (RDS) is one of the important causes of morbidity and mortality in preterm neonate's world over. Deficiency of surfactant in the lungs is the main cause of RDS. The risk of developing RDS is inversely related to the gestational age with the highest risk in babies with <28 weeks gestation and the least risk beyond 32-34 weeks. RDS complicates about 1% of pregnancies in USA. The incidence in India is reported to be 10-15% of all preterm births [1]. The combination of surfactant replacement therapy (SRT) with mechanical ventilation (MV) considered the standard of care appears to be falling out of favour due to the reportedly high morbidity with this approach [2,3]. Various approaches like bubble CPAP with binasal prongs (BCPAP), BCPAP with surfactant replacement, INSURE methods are non-invasive and gentle and are

being increasingly used to salvage preterm babies with RDS.

In the absence of sufficient surfactant, alveoli tend to collapse resulting in increase in work of breathing. CPAP provides continuous distending pressure to the alveoli and prevents their tendency to collapse, recruits more alveoli and conserves the endogenous surfactant. CPAP also stabilizes the chest wall and splints open upper airway reducing the airway resistance. The net effect of both exogenous surfactant administration and CPAP is increasing the functional residual capacity of the lungs. The efficacy of CPAP in RDS in reducing the need for invasive respiratory support is well documented [4, 5]. In developing countries like India, where surfactant administration is often not possible, early and judicious use of CPAP becomes an effective alternate intervention [6]. The

present study aims to study if usage of surfactant in addition to CPAP brings about a significant change in the outcome in preterms with RDS.

AIM AND OBJECTIVES

To determine the efficacy of CPAP alone verses CPAP with surfactant administration in moderate to severe RDS by comparing outcomes in both groups. The primary objective was successful weaning off without requiring MV.

MATERIALS AND METHODS

This is a retrospective study performed on preterm babies delivered at Gandhi hospital, Secunderabad between July 2016 and February 2017. One hundred and twenty preterm newborns with gestational ages between 28 and 32 weeks having moderate to severe RDS with Silverman Anderson score(SAS) greater than 3 admitted in neonatal intensive care unit were included in the study. Gestational age of the neonates was calculated based on LMP, antenatal ultra sound and New Ballard Score. Preterm neonates with less than 28wks of gestational age, severe HMD with SAS ≥ 7, prolonged and recurrent apnoea and those presenting with respiratory distress secondary to birth asphyxia, congenital anomalies of airway like choanal atresia, cleft palate, tracheo oesophageal fistula and congenital diaphragmatic hernia were excluded from the study. All preterm neonates presenting with respiratory distress in the first six hours of life were provisionally diagnosed as HMD. Routine investigations like CBP, CRP, Chest X ray are done for all the babies. Arterial blood gas analysis was done for babies whose SAS was between 4 to 6 with >60% FiO2 and PEEP >6. Surfactant was administered to such babies showing persistant hypercarbia (PaCo2 > 70mmHg) and or Ph <7.25, at the end of a sixty minutes of CPAP trial.

A total of 124 babies were recruited in the study. Forty two (33.8%) babies were managed on CPAP alone due to the non- availability of surfactant (group A). Eighty two (66.1%) babies were administered intra tracheal surfactant at a dose of 4ml/kg and were

continued on BCPAP (group B). CPAP was delivered using the Fisher and Paykel CPAP system. It comprises of a blender, a compressor and a humidifier connected to binasal prongs which form the interface between the circuit and the infant’s airway. The initial Positive end expiratory pressure (PEEP) was 5 cm of water and was later adjusted to obtain minimal retractions. The minimum and maximum PEEP was 4 & 7 respectively. Fio2 was started at 50% and was adjusted subsequently to maintain oxygen saturation (SpO2) between 88% and 92%. Once the target SpO2 is achieved and the work of breathing improved, FiO2 was gradually brought down to less than 30%. Flow of the gas was adjusted so as to produce continuous bubbling in the bubble chamber. Response to the intervention is studied by the improvements in SAS and SpO2. CPAP with or without SRT was considered successful if the respiratory distress as assessed by SAS decreased and baby could be successfully weaned off from CPAP within one week. The criteria for weaning were absence of respiratory distress (no retractions and respiratory rate between 30 and 60/min) ; Spo2 between 89% to 92% on an FiO2 of 30% and a PEEP of 4cmH2O. Babies were considered to have failed CPAP and were started on mechanical ventilation when they remained hypoxic with Spo2 <88% despite FiO2 >60% and pressure >7 cm of H2O and continuing to have retractions, grunting and recurrent apnoea.

All neonatal and CPAP variables like gestational age, birth weight, antenatal steroids, SAS, age of start of CPAP, initial FiO2, initial PEEP ,maximum FiO2, maximum PEEP, duration of CPAP and complications like sepsis, pneumothorax, nasal septal damage were compared between the two groups. Statistical analysis was performed using the SPSS statistics version 18.0 (SPSS Inc., Chicago, IL, USA). Chi-square test, t-test, and Wilcoxon rank-sum test were performed to compare demographic data, efficacy, and adverse effects. The results were considered statistically significant at P<0.05

RESULTS

Table-1: Demographics and clinical characteristics in two groups

Gestational age (weeks)	29.7±2.9	29.42±2.2	0.48
Sex(M:F)	27:15	53:29	0.76
Birth weight	1340±450	1290±438	<0.05
Antenatal steroids	29(69.04%)	59(71.9%)	0.51
Age at CPAP(hrs)	4±2.22	4.6±0.8	0.55
Age at Surfactant (hrs)	NA	5.4±0.8	
SAS	4.9±1.0	4.7±1.1	0.49
Initial Fio2	64±5.9	62±7.55	
Maximum PEEP	6.8±0.37	5.6±0.76	<0.05
Maximum Fio2 in %	75.7±10.2	64±7.3	<0.05
Duration of CPAP in hours	84.6±32.3	46.4±23.5	<0.05

Group a CPAP alone (n=42)

Group B CPAP+SRT (n=82)

P value Mean±SD

Table-2: Outcomes in CPAP vs CPAP+SRT groups

Sepsis	10	10	
Mechanical ventilation	8	6	<0.05
Pulmonary haemorrhage	4	2	<0.05
Pneumothorax	4	0	<0.05
Nasal septal damage	3	3	
Deaths	8	10	

Group A Outcomes CPAP alone (n=42)

Group B CPAP+SRT (n=82) p value

The study included data from 124 preterm babies with RDS treated in our institute during 2016 and 2017. Of them 42 patients were treated with CPAP alone (group A) and 82 patients were treated with CPAP and surfactant administration (group B). The mean gestational ages were 29.7 and 29.42 weeks, respectively. The male to female ratio was 64.51%/35.48% and there was uniform distribution in both the groups (CPAP: 64.28%/35.71%; CPAP with surfactant: 64.63%/35.36%). There were no statistically significant clinical differences between the groups in gestational age and duration before CPAP was initiated in both groups (Table 1). 26(61.9%) of babies from group A and 64(78%) of babies from group B could be successfully weaned off CPAP. The severity of respiratory distress and the percentage of oxygen required at the time of admission were comparable in both the groups. However, the maximum FiO₂ required, the maximum PEEP and the duration of CPAP was significantly higher in group A than in group B. We further studied the incidence of complications in both groups. There were eight deaths including two babies who required mechanical ventilation in group A whereas there were 10 deaths in group B. Group A had higher incidence of pulmonary haemorrhage and pneumothorax (Table 2).

DISCUSSION

The present study is a retrospective study done with an objective to compare the efficacy of CPAP versus CPAP with surfactant in reducing the respiratory distress in hyaline membrane disease. The number of patients in both groups was different. There were no statistically significant clinical differences between the groups regarding when the treatment was initiated. In the group which received CPAP along with surfactant, 78% could be weaned off whereas 61.9% from the CPAP only group could be weaned off. The difference is statistically significant. In a comparative study done by El-Masry *et al.* the success rate in both the groups was high and there was significant difference in favour of CPAP with surfactant [7]. The lower success rate of CPAP alone in our study compared to that of El-Masry *et al.* could be due to the delayed institution of CPAP. The duration on CPAP was shorter in group B compared to group A. This was in contrast with the findings from El-Masry *et al.* who found no difference in the duration of CPAP. Analysis of outcomes revealed significant failures in group A with more babies requiring MV. This

is in contrast with the results of other studies which found no statistical difference in the incidence of MV in both groups [7, 8]. Further, we experienced a higher incidence of pneumothorax and pulmonary haemorrhage compared to the other studies [8].

Our results suggested that the CPAP with surfactant therapy was superior to CPAP alone in improving the respiratory distress and reducing the need for MV. A recent review suggests early use of CPAP with early rescue surfactant as the ideal approach for management of respiratory distress syndrome in preterm infants [6]. Reininger *et al.* compared the effect of one dose of intratracheally administered surfactant followed by extubation to nasal continuous positive airway pressure (NCPAP) and compared it to NCPAP alone. They concluded that surfactant administration reduces the need for later mechanical ventilation [9]. In our study we found surfactant administration to be effective in reducing the need for later MV. The Von DRM trial concluded that preterm neonates initially managed with either n CPAP or prophylactic surfactant with rapid extubation to n CPAP had similar clinical outcomes to those treated with prophylactic surfactant followed by a period of mechanical ventilation. An approach that uses early n CPAP leads to a reduction in the number of infants who are intubated and given surfactant [10]. The study group of Dunn *et al.* was between 26 and 29 weeks of GA. Our study population was more mature in both the groups. Prophylactic surfactant could not be used in our study. We found that though CPAP alone may be of benefit in reducing respiratory distress, addition of surfactant is significantly more beneficial. Management with CPAP alone is comparatively cheaper than CPAP plus SRT. More over the present consensus is in favour of CPAP with early rescue surfactant in babies with respiratory distress [11].

Ours is a retrospective study. A prospective study would have given a better answer. Our observations brought out the following, though results of CPAP with surfactant group were better, it can be understood that CPAP is invaluable in the management of neonatal respiratory distress syndrome. Addition of surfactant definitely improves the chances of survival for babies with RDS.

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