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Original Research Article

Study of respiratory distress syndrome in newborn with special reference to the role of bubble CPAP in its management

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ABSTRACT

Background: Respiratory distress syndrome is the most important cause of morbidity and mortality in preterm neonates. Intermittent positive pressure ventilation with surfactant therapy was standard treatment of RDS. IIPV is invasive, costly and requires expertise. It is not a viable option for many of the resource limited SNCU set ups of our country. Trials have showed that CPAP is noninvasive, easy to use, safe and effective. This study was done to find out effectiveness of CPAP in RDS, and also to find CPAP failure factors.
Methods: This was a prospective observational study, carried out at SNCU of Dhiraj hospital, Piparia, Vadodara district, Gujarat, India form February 2014 to March 2015. Neonates with diagnosis of respiratory distress syndrome were included in this study.
Results: Total 57 (42 inborn and 15 out born) cases of RDS were analyzed in this study. Incidence of RDS was 3.68% of live births. 5(8.8%) settled down with low flow oxygen only. 24 (42.1%) successfully treated with CPAP only. 15 (26.3%) were treated with CPAP and surfactant. 13 (22.8%) were CPAP failure cases which required ventilator support. The variables significantly associated with failure of CPAP were: no exposure to antenatal steroids (p value of 0.025), grade 3-4 RDS on CXR (p value of 0.03), PDA (p value of 0.0264), sepsis/pneumonia (p value of <0.001) and Silverman Anderson score of ≥7 at admission (p value of 0.001). 3 (5.3%) went on DAMA. 5 (8.8%) expired and 49 (85.9%) were discharged. 4 out of 5 (80%) death occurred in very preterm group. 4 (80%) of death occurred in neonates whose mothers did not receive any dose of antenatal steroid. There was no mortality in neonates who were in need of surfactant and received within 6 hours of life. 75% of neonates having sepsis and asphyxia both along with RDS expired.
Conclusions: Bubble CPAP is safe and very effective in low resource settings. CPAP failure is significantly associated with no antenatal steroids, grade 3 to 4 x-ray changes of RDS, Silverman Anderson score of ≥7 at beginning of CPAP, presence of significant PDA and association of sepsis/pneumonia.

Keywords: Bubble CPAP, CPAP failure, RDS

INTRODUCTION

Respiratory distress syndrome is the most important cause of morbidity and mortality in preterm neonates. According to the year 2002-03 report of National neonatal perinatal database (NNPD), incidence of RDS in India was 1.3% of all live births and it was the primary cause of death in 13.5%.[1] The incidence of RDS is

inversely related to gestational age. In babies born at 28-32 weeks, RDS occurs in up to 50% of births.[2] Intermittent positive pressure ventilation with surfactant therapy was standard treatment of RDS. The major difficulty with IIPV is that it is invasive, results in lung injury with increased risk of ventilator associated pneumonia and chronic lung disease. It is costly as well, and meticulous nursing care is required with expertise. It is not a viable option for many of the resource limited SNCU set ups of our country. Continuous positive airway pressure (CPAP), refers to the application of continuous distending pressure in a spontaneously breathing neonate, increases the functional residual capacity of lung resulting in better gas exchange.[3]

Many trials have showed that it is noninvasive, easy to use, safe and effective of managing RDS cases. Benefits of CPAP have made CPAP the standard of care in managing sick preterm neonates with RDS in high income countries.[4] This study was done to find out effectiveness of CPAP in RDS cases, and also to find CPAP failure factors. So that guidelines can be set about kind of cases to be managed at a particular SNCU facility having CPAP as only way of providing respiratory support.

METHODS

This was a prospective observational study, carried out at SNCU of Dhiraj hospital, Piparia, Vadodara district, Gujarat, India form February 2014 to March 2015. Neonates with diagnosis of respiratory distress syndrome were included in this study.

Inclusion criteria

- All the neonates with signs and symptoms of respiratory distress, Silverman score of >3 within 6 hours of life and CXR suggestive of RDS
- Birth in Dhiraj hospital, or outside births who are admitted within 6 hours of life.

Exclusion criteria

- Neonates admitted after 6 hours of life
- Neonates weighing less than 800 grams were excluded from trial of CPAP.

Neonates with Silverman score of more than 3 with head box oxygen requirement of more than 3 liters/minute (approx. 30% FiO_2) to maintain SpO_2 of more than 90% were put on bubble CPAP with nasal prongs (Fisher and Paykel).

They were started with PEEP of 5 cm H_2O and FiO_2 with 30% (increased to 40% to keep SpO_2 of more than 90%). At a point when if neonate who failed to maintain SpO_2 with PEEP of 5 cm H_2O and FiO_2 of 40% were advocated surfactant therapy (NEOSURF, CIPLA at 5ml/kg) and were put back again on CPAP (INSURE technique). Thereafter, if required PEEP was increased to max of 7 cm H_2O and FiO2 of max 60% in order to maintain SpO_2 more than 90% with minimal distress.

CPAP failure is considered when

- Neonate is in need of CPAP >7 cm H2O with FiO_2 > 60%
- More than 2 episodes of apnea requiring bag and mask ventilation
- Shock.

Neonates were monitored continuously. Routine blood investigations and CXR were done in all investigations, and repeated as and when required. ABGs were done very infrequently because of cost factor. Supportive management was provided as per standard protocols.

RESULTS

During study period, total number of live births was 1143, of which 938 were full term and 205 were preterm neonates.

None of the full-term neonate developed RDS. 42 out of 205 premature neonates developed RDS. Total number of neonates included in this study was 57, which comprised 42 in born neonates and 15 out born neonates.

Gestational age wise distribution of RDS cases

Incidence of RDS was 3.68% (42 neonates out of 1143 live births). Rate of RDS was 89% in very preterm, 70% in moderate preterm, 3.2% in late preterm and no in full term neonates (Table 1).

Table 1: Gestational age wise distribution of RDS cases.

	No. of live births	No. of RDS cases inborn	RDS cases out born	Total RDS cases
<28 weeks	00	00	00	00
28-32 weeks	18	16 (89%)	10	26 (45.6%)
32-34 weeks	30	21 (70%)	03	24 (42.1%)
34-37 weeks	157	5 (3.2%)	02	07 (12.3%)
>37 weeks	938	0 (0%)	00	00
	1143	42 (3.68%)	15	57 (100%)

Birth weight wise distribution of RDS cases

3 (5.2%) cases were extremely low birth weight. 29 (50.9%) were very low birth weight. 25 (43.9%) were low birth weight, of which 23 were between 1500-1999 grams and 2 were above 2000 grams (Table 2).

Table 2: Birthweight wise distribution of RDS cases.

Birth weight	RDS cases
< 1000 gm	3 (5.2%)
1000-1499 gm	29 (50.9%)
1500-1999 gm	23 (40.3%)
>2000 gm	2 (3.6%)
Total	57 (100%)

Table 3: Risk factors for RDS.

Risk factor	Number of RDS cases
Prematurity	57 (100%)
Male Sex	34 (59.6%)
LSCS delivery	16 (28%)
Maternal Diabetes	03 (5.2%)
Multiple births	02 (3.5%)
Perinatal asphyxia	08 (14%)
Family history of RDS in sibling	01 (1.75%)
Induced Labour	12 (21%)

Risk factors for RDS

Presence of known risk factors associated with RDS were premature birth (100%), male gender (59.6%), LSCS delivery (28%), induced labour (21%), perinatal asphyxia (14%), maternal diabetes (5.2%), multiple births (3.5%) and history of sibling affected with RDS (1.75%) (Table 3).

Radiological grading of RDS

Based on CXR findings 43 (75.4%) of cases were mild to moderate cases with radiological findings of grade 1 to 2 changes. 14 (24.6%) were severe cases with radiological findings of grade 3 to 4 (Table 4).

Modes of management

Out of 57 neonates with RDS, 5(8.8%) settled down with low flow oxygen only. 24 (42.1%) successfully treated with CPAP only. 15 were treated with CPAP and surfactant. 13 (22.8%) were CPAP failure cases which required ventilator support. Surfactant was given in 18 cases. Another 18 neonates were advised for surfactant, but were not affording for that, and so was not given (Table 5).

Table 4: Radiological grading of RDS.

CXR	Number of RDS cases
Grade 1-2	43 (75.4%)
Grade 3-4	14 (24.6%)

Table 5: Modes of management.

Mode of management		RDS cases
Oxygen		05 (8.8%)
CPAP		24 (42.1%)
CPAP + surfactant		15 (26.3%)
CPAP failure	Ventilator	10 (17.5%)
	Ventilator + surfactant	03 (5.3%)

Table 6: Risk factor based comparison of CPAP success and CPAP failure.

	CPAP success (n=39)	CPAP failure (n=13)	P value
Birthweight (gm) (mean ±SD)	1.36±0.289	1.55±0.38	0.070
Gestational Age (wk) (mean ±SD)	31.00±1.85	31.85±2.51	0.1999
Mean duration of stay	26.74±11.99	34.62±13.7	0.105
Male sex	22 (56.4%)	10 (77%)	0.321
Birth weight < 1500 gm	20 (51.3%)	11 (84.6%)	0.073
Gestational Age < 32 weeks	16 (41%)	10 (77%)	0.084
Antenatal steroids taken	22 (56.4%)	02 (15.4%)	0.025
Grade 3-4 on CXR	07 (17.9%)	07 (53.8%)	0.030
Silverman score ≥ 7	10 (25.6%)	11 (84.6%)	<0.001
Sepsis/pneumonia	05 (12.8%)	09 (69.3%)	<0.001
Severe Birth asphyxia	05 (12.8%)	03 (23.1%)	0.654
PDA	03 (7.7%)	05 (38.5%)	0.0264
Maternal hypertension	18 (46.1%)	04 (30.8%)	0.16
Intramural delivery	29 (74.3%)	08 (61.5%)	0.34

Risk factor based comparison of CPAP success and CPAP failure

Out of 52 neonates who were supported with CPAP to begin with, 39 (were successfully treated with CPAP (75%). 13 (25%) had CPAP failure.

The variables significantly associated with failure of CPAP were: no exposure to antenatal steroids (p value of 0.025), grade 3-4 RDS on CXR (p value of 0.03), PDA (p value of 0.0264), sepsis/pneumonia (p value of <0.001) and Silverman Anderson score of ≥7 at admission (p value of 0.001) (Table 6).

Outcome of neonates

Out of 57 cases, 3 (5.3%) went on DAMA. All 3 were CPAP failure cases. 5 (8.8%) expired and 49 (85.9%) were discharged (Table 7). Factors contributing for mortality (Table 8).

Table 7: Outcome of neonates.

	Total RDS cases (N=57)
Discharged	49 (85.9%)
Dama	03 (5.3%)
Expired	05 (8.8%)
Total	57

Table 8: Factors contributing for mortality.

	RDS cases excluding dama (n=54)	Mortality (n=5)
Gestational age		
<28 weeks	00	00
28-32 weeks	23	04 (17.4%)
32-34 weeks	24	01 (4.2%)
34 -<37 weeks	07	00 (0%)
Birth weight		
<1000 gm	01	01 (100%)
1000-1499 gm	28	03 (10.7%)
1500-1999 gm	23	01 (4.4%)
≥2000 gm	02	00 (0%)
CXR grading of RDS		
Grade 1- 2	41	02 (4.88%)
Grade 3-4	13	03 (23.1%)
Antenatal steroids		
None	28	04 (14.3%)
Single dose betamethasone	14	01 (7.14%)
Two doses of betamethasone	12	00 (0%)
Surfactant		
Given <6 hours of life	10	00 (0%)
Given >6 hours of life	07	01 (14.3%)
Not affording	18	04 (22.2%)
Not required	19	00 (0%)
Sepsis and asphyxia		
Sepsis	12	04 (33.3%)
Asphyxia	08	02 (25%)
Sepsis and asphyxia	04	03 (75%)
Place of delivery		
Intramural	40	03 (7.5%)
Extramural	14	02 (14.3%)

DISCUSSION

Total number of neonates included in this study was 57, which comprised 42 in born neonates and 15 out born neonates. Incidence of RDS was 3.68% (42 neonates out of 1143 live births). Rate of RDS was 89% in very preterm, 70% in moderate preterm, 3.2% in late preterm and no in full term neonates. Sun H et al conducted a retrospective study from January 2006 to December 2010 and found that the incidence of RDS was inversely proportional to gestational age and caesarean section without labor was significantly associated with RDS in

term and late preterm infants (p <0.001).[5] In present study, risk factors associated with RDS were premature birth (100%), male gender (59.6%), LSCS delivery (28%), induced labour (21%), perinatal asphyxia (14%), maternal diabetes (5.2%), multiple births (3.5%) and history of sibling affected with RDS (1.75%). In an epidemiological survey done by Liu L common risk factors were 33.1% cases of birth asphyxia, 19.7% cases of multiple births, 17.8% cases of gestational hypertension, 15.2% cases of fetal distress, 13.7% cases of premature rupture, 5.7% cases of placental abruption, 1.6% cases of gestational diabetes, 1.4% cases of intrahepatic cholestasis in pregnancy.[6]

Out of 52 neonates who were supported with CPAP to begin with, 39 (were successfully treated with CPAP (75%). 13 (25%) had CPAP failure. The variables significantly associated with failure of CPAP were: no exposure to antenatal steroids (p value of 0.025), grade 3-4 RDS on CXR (p value of 0.03), PDA (p value of 0.0264), sepsis/pneumonia (p value of <0.001) and Silverman Anderson score of ≥7 at admission (p value of 0.001). In a retrospective study by Ammari et al., the failure rate of bubble CPAP was 24% in babies <1250 grams and 50% in babies <750 grams. None of the babies with gestational age >30 weeks failed CPAP. The predictors of CPAP failure were need for positive pressure ventilation at birth, alveolar to arterial oxygen difference >180 mmHg on first blood gas and severe RDS on initial chest x-ray.[7] In a systematic review done by Stevens TP et al., comparing INSURE with ventilation, CPAP failure rate ranged from 14 to 40%. The difference may be attributed to birth weight and gestational age of infants enrolled, type of nasal interface, the CPAP device, age of starting CPAP, and use of antenatal steroids and surfactant.[8] In a case controlled study by Boo et al., of the 97 preterm with RDS on ventilator CPAP or Bubble CPAP, 38% failed CPAP and required ventilator support. Only 34% of infants in their study received antenatal steroids. Similar to our study severe RDS on chest x-ray was an important predictor of CPAP failure.[9]

In present study, out of 57 cases, 3 (5.3%) went on DAMA. All 3 were CPAP failure cases. 5 (8.8%) expired and 49 (85.9%) were discharged. Risk of mortality was high in lower gestational age very preterm neonates. 4 out of 5 (80%) death occurred in this group. Mortality rate was high among lower birth weight group. In present study 100% of ELBW neonates with RDS expired. 10.7% (3 out of 28) of VLBW neonates expired, which accounted for 75% (3 out of 5) of deaths due to RDS. A study done by Chard T et al., who conducted study on 255 neonates born between 22-36 weeks of gestation and concluded that the risk of RDS and neonatal death does not appear to be related to the birth weight of preterm neonates, but is of course related to gestational age.[10] Fehlmann et al. conducted a descriptive study using data from 20 hospitals in South America including 5991 very low birth weight neonates and proved that RDS had a high incidence in very low birth weight infants, despite the frequent use of antenatal steroids. VLBW infants had a higher mortality and an increased risk of relevant morbidity.[11]

Present study shows that of the 28 mothers who did not receive any antenatal steroids; 4 (14.3%) of their babies expired. Of the 14 mother who received single dose of antenatal steroid 1 (7.1%) expired and no mortality was seen for the 12 babies whose mother had received two doses of steroids. Systematic review done by Men Jean lee at al., on pregnant women at high risk for preterm delivery before 37 weeks of gestation randomly assigned to receive two doses of betamethasone or placebo showed that administration of betamethasome resulted in lower incidence of RDS (9.0 versus 25.8 percent in controls). The maximum benefit occurred in subgroup of infants delivered more than 48 hours but less than seven days after maternal treatment (incidence of RDS: 3.6 versus 33.3 percent in controls), and when the drug was given between 26 and 32 weeks of gestation (incidence of RDS: 11.8 versus 69.6 percent in controls).[12]

Present study shows that out of the 10 neonates who received surfactant within 6 hours of life showed no mortality. Of the 7 neonates who received surfactant after 6 hours of life, 1 (14.3%) expired. Of the 18 neonates who were not affording for surfactant but were in need 4 (22.2%) expired. Of the 19 neonates who were not in need for surfactant showed no mortality. Henrik Varder et al. conducted a study on 68 infants with moderate to severe respiratory distress. 35 infants were given surfactant and nasal CPAP and 33 were given only CPAP. They found less subsequent need for mechanical ventilation in infants treated with surfactant.[13]

In the present study, it was noted that presence of sepsis and/or asphyxia carries increased risk of mortality. 33.3% of neonates with comorbid sepsis expired. 25% of neonates with associated asphyxia expired. Presence of both sepsis and asphyxia carries poor outcome with 75% risk of mortality.

Mortality rate was higher in extramural cases (14.3%) as compared to 7.5% in intramural cases. The probable cause behind it may be inadequate resuscitation, inadequate care during transport and relatively late initiation of appropriate management. In our study, air leak and pneumothorax developed in 3 (5.76%) cases.

CONCLUSION

Early institution of bubble CPAP in management of RDS can significantly reduce the need for mechanical ventilation and surfactant therapy. It is safe and very effective in low resource settings. Success rate of CPAP is quite high good monitoring, supportive care and nursing care is provided. CPAP failure is significantly associated with no exposure to antenatal steroids, grade 3 to 4 x-ray changes of RDS, Silverman Anderson score of

≥7 at beginning of CPAP, presence of significant PDA and association of sepsis/pneumonia.

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REFERENCES

1. National Neonatal Perinatal Database 2002-03, NNPD Network. Supported by Indian Council of Medical Research, New Delhi, Nodal Center, AIIMS, New Delhi. http://www.newbornwhocc.org/pdf/nnpd_2002-03.PDF
2. Lemons JA, Bauer CR, Oh W, Korones SB. Very low birth outcomes of the National Institute of Child Health and Human development neonatal research network. Pediatrics. 2001;107(1):E1.
3. Gregory GA, Kitterman JA, Phibbs RH, Tooley WH, Hamilton WK. Treatment of idiopathic respiratory distress syndrome with continuous positive airway pressure. N Engl J Med. 1971;284(24):1333-40.
4. Thukral A, Sankar MJ, Chandrasekaran A, Agarwal R and Paul VK. Efficacy and safety of CPAP in low and middle-income countries. J Perinatol. 2016;36:S21-8.
5. Sun H, Xu F, Xiong H, Kang W. Characteristics of respiratory distress syndrome in infants of different gestational ages. Lung. 2013;191(4):425-33.
6. Liu L. Epidemiological survey of neonatal respiratory distress syndrome in part of northwest regions in China. Zhonghua Er Ke Za Zhi. 2015;53(5):341-7.
7. Ammari A, Suri M, Milisavljevic V, Sahni R, Bateman D. Variables associated with the early failure of nasal CPAP in very low birth weight infants. J Pediatr. 2005;147(3):341-7.
8. Stevens TP, Harrington EW, Blennow M, Soll RF. Early surfactant administration with brief ventilations versus. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. Cochrane Database Sys Rev. 2007;4:CD003063.
9. Boo NY, Zuraidah AL, Lim NL, Zulfiqar MA. Predictors of failure of nasal continuous positive airway pressure treatment of preterm infants with respiratory distress syndrome. J Trop Pediatr. 2000;46:172-5.
10. 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(9):523-6.
11. Fehlmann E Tapia JL, Fernandez R, Bancalari A. Impact of respiratory distress syndrome in very low birth weight infants: multicenter South American study. Arch Argent Pediatr 2010;108(5):393-400.
12. Men-Jean Lee. Antenatal corticosteroid therapy for reduction of neonatal mortality and morbidity from preterm delivery. Cochrane Database Sys Rev. 2006:CD004454.
13. Verder H, Robertson B, Greisen G, Ebbesen F, Albertsen P, Lundstrom K, et al. Surfactant therapy and nasal continuous positive airway pressure for newborns with respiratory distress syndrome. New Engl J Medicine. 1994;331(16):1051-5.

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