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Original Research Article

Factors influencing the respiratory support in low birth weight neonates: A clinical study in tertiary care teaching hospital

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Abstract

Background: Deficiency of pulmonary surfactant is one of the most important factors contributing to the development of respiratory RDS [1]. In immature lungs, the elevated surface tension resulting from surfactant deficiency leads to alveolar collapse at the end of expiration, atelectasis, uneven inflation and regional alveolar over distension. Improved use of antenatal steroids, labour room CPAP, trial of CPAP before intubation and caffeine have changed the way a preterm baby with RDS is managed in the last decade. Many babies with RDS who used to receive prophylactic or early rescue surfactant are now managed with CPAP alone, others are administered surfactant only if they fail CPAP. But, in this process of trial of CPAP, a few babies receive surfactant as "late rescue" after few hours of trial of CPAP. Objective: To evaluate factors determining long duration of respiratory support (CPAP/ventilation > 120 hours) in VLBW babies in Indian NICU.

Aims and Objectives: To evaluate factors determining long duration of respiratory support (CPAP/ventilation > 120 hours) in VLBW babies in Indian NICU.

Material and Methods: A prospective longitudinal study was conducted at RDJM Medical College, Muzaffarpur, Bihar, India from October 2021 to September 2022. All legally viable preterm babies < 32 weeks and < 1500 grams (inborn or out born admitted within 2 hours of birth) were included in the study. A total of 50 Babies were included in the study.

Results and Observations: Out of 50 babies 9 babies were excluded from analysis due to major malformation in 6 and referral of 3 cases. A definite association was noted between gestation (86% of<28 weeks 46% of 29-30, 18% of 31-32 weeks babies, p=0.02) and long duration of respiratory support. Boys vs girls (61% vs 32%, p=0.06), babies born after spontaneous labor vs delivery for maternal/fetal reasons (67% vs 32%, P0.06) were likely to require long duration of respiratory support.

Conclusion: Early institution of CPAP in the management of RDS in premature neonates, can significantly reduce the need for MV & surfactant therapy. 50% babies of very preterm babies required no/minimum respiratory support of <24 hours Babies needing intubation before trial of CPAP, babies preterm labor and with hsPDA are associated with long duration respiratory support.And also, large scale Randomized controlled trials (RCTS) are warranted

Keywords: CPAP, VLBW babies, neonates, low birth weight, factors influencing, respiratory support

Introduction

Deficiency of pulmonary surfactant is one of the most important factors contributing to the development of respiratory RDS [1] In immature lungs, the elevated surface tension resulting from surfactant deficiency leads to alveolar collapse at the end of expiration, atelectasis, uneven inflation and regional alveolar over distension. If untreated, this will result in epithelial injury and pulmonary edema which further interfere with surfactant function, producing the clinical picture of RDS [2]. Lower the gestation, higher is the incidence of RDS, accounting for nearly 80% incidence in preterm infants with gestation less than 28 wk.

Improved use of antenatal steroids, labour room CPAP, trial of CPAP before intubation and caffeine have changed the way a preterm baby with RDS is managed in the last decade [3]. Many babies with RDS who used to receive prophylactic or early rescue surfactant are now managed with CPAP alone, others are administered surfactant only if they fail CPAP[4, 5]. But, in this process of trial of CPAP, a few babies receive surfactant as "late rescue" after few hours of trial of CPAP. Previous studies have addressed the tiniest of babies who are at high risk of CLD and hence, not intubating is critical. In India we manage mostly babies > 28 weeks and > 1000 grams. Hence, the incidence of CLD isn't high. Studies from India [6] have shown that surfactant followed by CPAP may be a better approach than CPAP trial followed by late surfactant. Interventions to prevent RDS should begin before birth and involve both paediatricians and obstetricians as part of the perinatal team. Often there is prior warning of impending preterm delivery, allowing time for interventions to be considered including in utero (maternal) transfer where appropriate. Ultrasound examination of cervical length and testing for the presence of fetal fibronectin in vaginal secretions can help to predict the risk of preterm birth [7]. Preterm babies at risk of RDS should be born in centres where appropriate skills are available for stabilization and ongoing respiratory support, including intubation and mechanical ventilation (MV) if indicated. Long-term health outcomes for extremely preterm babies are better if they receive their initial neonatal care in tertiary units. It is possible that some of the babies who are given surfactant late, after a trial of CPAP have milder RDS and this approach is appropriate. On the contrary, it is biological sense that denial/delaying surfactant, may be prolonging the naturally history of RDS. In this analytic study, we evaluate the determinants of "duration of ventilation" in VLBW babies in an Indian tertiary NICU, with primary interest in timing of surfactant. Although death/CLD is an ideal patient relevant outcome, longer hours (>120 hours in our study) are associated with risks of infection, mandate cost intensive device and skilled manpower use; and is an important outcome in a country like India where most of health care is not state sponsored, and family pays.

Material and Methods

A longitudinal prospective study was done in RDJM Medical College, Muzaffarpur, Bihar, India from October 2021 to September 2022. All legally viable preterm babies < 32 weeks and < 1500 grams which were delivered in the same hospital or referred from other hospital or admitted in the NICU of the Hospital within two hours of delivery who required surfactant administration were included in the study. Inclusion criteria: All legally viable preterm babies < 32 weeks and < 1500 grams (inborn or out born admitted within 2 hours of birth). Exclusion criteria 1. Babies with associated surgical illness 2. babies < 24 weeks gestation and < 400 grams birth weight) All legally viable babies (>23 weeks and >400 grams) are offered optimal resuscitation and NICU care, we do not withhold ventilation or surfactant, if

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clinically indicated. Most of the preterm births are a planned activity, the obstetrician and neonatology team prepare for optimal care of a VLBW baby. Eligible babies included in the study were treated for respiratory distress according to unit's standardized respiratory care policy. Data was collected prospectively for survival, duration of CPAP/ventilation, and all the determinants like gestation, weight, sex, antenatal steroids (ANS), cause for preterm birth (spontaneous preterm labor or planned delivery for maternal/fetal indication), ventilator associated pneumonia (VAP) and patent ductus arteriosus (PDA).

Surfactant policy

1. We do not administer prophylactic surfactant (in labor room, before onset of respiratory distress).
2. If a preterm baby (30% after a trial of effective CPAP (for 1-2 hours after stabilization). This decision is taken by the treating team of residents and consultant. Data was entered in excel sheet and analyzed using SPSS v 20 and analyzed.

Results and Observations

In our study a total of 50 eligible babies were enrolled during the study period, out of the 50 cases 9 cases were excluded (6 due to major malformation and 3 was referred to another hospital). Hence a total of 41 babies were enrolled for the study.

Table 1: Baseline features of the cases

	Features	Frequency (n= 41)	Percentage(%)
	≤ 28 weeks	7	17
Gestational Age	29-30 weeks	17	41.5
	31-32 weeks	17	41.5
	< 1000 grams	11	26.8
Birth weight	1001-1250	17	41.5
	1251-1500	13	31.7
Gender	Boys	24	58.5
	Girls	17	41.5
Presentation	Intramural	39	95.1
	Extramural	2	4.2
Mode of Delivery	FTND	7	17.1
	LSCS	34	82.9

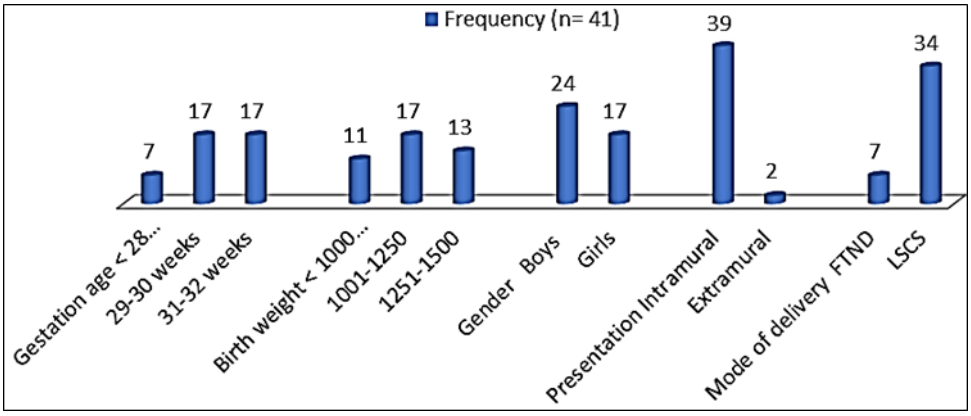

Fig1: Baseline features of the cases

The mean gestational age of the babies in the study group was 29.6 +1.8 weeks in our study,

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with majority of them (83%) had crossed 28 weeks of gestation. Nearly 41.5% of the babies weighed between 1001-1250 gms, 31.7% weighed more than 1250 gms. The mean birth weight of babies in our study was 1150+ 217 gms. Boys constituted nearly 58.5% of the study population. Nearly 95.1% present with intramural and 82.9% of the babies were delivered by LSCS As in Table 1and figure 1.

Table 2: Clinical Characteristics of the neonates

	Features	**Frequency (n= 41)**	**Percentage(%)**
Cause of prematurity	PTOL/PPROM (risk of EONS)	16	39
	Maternal/Fetal Indication	25	61
Need for resuscitation	None	19	46.3
	Initial steps	4	9.8
	Intubation	18	43.9
ANS	Completed	26	63.4
	Incompleted/No	15	36.6
PPV in LR	None	12	29.3
	T piece	26	63.4
	Self-inflating bag	3	7.3
	LR for resuscitation	18	43.9
Intubation	Early rescue surfactant	17	41.5
	Late rescue surfactant	6	14.6
	Not ventilated	12	29.3
Hypocarbia events	CO_2 always > 30	22	53.6
	CO_2< 30	5	12.2
	Missed number of ABGs	2	4.8
	Not ventilated	12	29.3
	PaO_2< 80 Spo2 always<95	22	53.6
Hyperoxia	PaO_2> 89/saturations > 95 for more than 6 hrs	5	12.2
	Missed number of ABGs	2	4.8
CRP positive (>10MG/L)/Culture proven sepsis	Yes	8	19.5
Clinical sepsis	Antibiotics used more than 5 days	10	24.4
	No sepsis	31	75.6

16 babies (39%) had risk of EONS, were delivered premature due to preterm labor/rupture of membranes, others for maternal or fetal indications. 26 (63.4%) babies received a complete course of ANSand 14 one dose (34.1%). We have very high compliance to ANS for anticipated preterm birth. Intubation was done in 43.9% of the babies for the purpose of resuscitation.18 (44%) babies received LR CPAP. 17 (41.5%) babies received Early rescue surfactant (within 2 hours) and 6 (14.6%) babies received surfactant later. Nearly 53.6% of the babies had Co2 of more than 30 always. the oxygen saturation of more than 89-95% for more than 6 hours was seen in nearly 12.2% of the individuals. 19.5% of the babies had CRP positive for the culture proven sepsis and nearly 24.4% of the babies received Antibiotics for more than 5 days As in Table 2.

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Table 3: Respiratory support required in the cases

Type of support	Number (%)
Respiratory care in labor room	
LRCPAP	18(44%)
Intubation in Labour room	9(22%)
Need for respiratory support in NICU	
No need of respiratory support	10(24%)
<24hours intubation/CPAP	14(34%)
Need for >120 hrs respiratory support	12(29%)

18 (44%) babies received LR CPAP, 9 (22%) babies required intubation in LR. 10 babies (24%) required no respiratory support. Half the babies required brief respiratory support-6 (14%) babies were managed on CPAP alone, 14 (34%) babies required less than 24 hours of intubation. 17 babies received Early rescue surfactant (within 2 hours) and 6 babies received surfactant later. 2 babies died, 3 babies developed CLD (12% death/CLD). 12 (29%) babies required more than long duration (ventilation/CPAP > 120 hours) of respiratory support. As in Table 3.

Table 4: Factors determining need for Long Respiratory Support

Type of support	Number (%)	Need for respiratory Support>120Hrs	P value
Gender	Boy	61%	0.06
	Girl	32%	
Cause for delivery	PPROM/PTOL	67%	0.06
	Delivered for maternal/fetal cause	32%	
Type of initial support	Intubation in LR	60%	0.03
Required	CPAP given	18%	
PDA	hs PDA	86%	
	Non-significant/no PDA	33%	0.02

As in Table 4, A definite association was noted between gestation (86% of <28 weeks, 46% of 29-30, 18% of 31-32 weeks babies, p=0.02) and long duration of respiratory support. Boys vs girls (61% vs 32%, p=0.06), babies born after spontaneous labor vs delivery for maternal/fetal reasons (67% vs 32%, P0.06) were likely to require long duration of respiratory support. Babies requiring intubation before trial of CPAP (60% vs 18%, p=0.03) required long duration respiratory support. This may merely be a reflection that these babies had a more severe RDS to begin with. Support/coin trials where babies were randomized trials, to early intubation or CPAP trail before intubation. Our respiratory care policy was to try CPAP if babies were not intubated in LR for resuscitation or for severe apnea. Babies with hsPDA (86% vs 33%, p=0.02) (7 babies were treated for ECHO proven hsPDA). In our unit, ECHO was performed only when PDA was suspected clinically based on poor perfusion or unresolving RDS. ECHO was performed by pediatric cardiologist, we do not do clinician performed ECHO for all these very preterm babies. Hence, this association may also be biased. We found no increase in death/CLD or duration of respiratory support in babies who received surfactant late, after a trial of CPAP. Following factors had no association with long duration of respiratory support in our study-birth weight of baby, doses of antenatal steroids, mode of delivery, timing of surfactant, risk of EONS or VAP. 8 babies had CRP/culture positive sepsis, in 10 babies possibility of infection couldn't be excluded as antibiotics were continued/upgraded as more respiratory support was required, although infection markers were absent.

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Discussion

Dunn *et al*., in one of the very early preliminary report on Use of the 'Gregory box' (CPAP) in treatment of RDS of the newborn have reported lesser mortality with CPAP compared to existing methods.Bassiouny*et al*. in their study of Forty-four premature infants with RDS, treated with binasal, have reported the incidence of CPAP failure as 39% and significant improvement of RDS with a mild to moderate degree of severity on CPAP. They have also reported significantly lower incidence of infection, apnea, intraventricular hemorrhage and retinopathy of prematurity with CPAP. No pneumothorax was reported in the study.

A total of 41 babies with pre-maturity were analyses in our study. Increasing numbers of very preterm and VLBW infants are surviving because of advances in both perinatal and neonatal care over the past two decades [8]. The mean age of gestation in our study was 29.6 weeks among the premature mothers and mean birth weight was 1150 gms. The findings of our study was similar to the study findings of Daynia E Ballot *et al*.[9] where age of gestation was 29.9 weeks of pregnancy with mean birthweight of 1133.5 gms. In the study done by DenizAtalay*et al*. [10] the preferred mode of delivery followed was LSCS for 89.7% of the subjects which is similar to our study findings. In many cases, obstetrician-gynecologists teamed with neonatologists and contributed to saving ELBW infants, by delivering them via CS, thereby favorably influencing the outcome for the newborn [11]. Minguez-Milio*et al*.[12] reported that delivery mode did not affect survival; however, delivery via CS was associated with lower morbidity and better prognosis for neurodevelopmental long-term outcome in ELBW infants. Nearly 52% of the study participants required resuscitation soon after birth in our study which is also similar to the study fidnings of DenizAtalay*et al*. The sepsis was seen in nearly 19.15 of the babies in our study where in Deniz study sepsis was seen in nearly 80% of the babies. CPAP can be delivered via a face mask or a shortened endotracheal tube taped into the nasopharynx [13]. T-piece devices enable a controlled delivery of a set background CPAP with a measured peak inspiratory pressure. If lung inflation is needed a single sustained inflation of about 25 cm H_2O for about 15s may be better than repeated manual inflations, although more research is needed for this intervention[14]. Self-inflating bags do not require a pressurized gas supply to deliver air flow but cannot deliver CPAP, and the peak inspiratory pressure cannot be controlled beyond the use of the safety valve, which is usually set at about 40 cm H_2O. Flow inflatingbags cannot deliver accurate CPAP and even in experienced hands produce variable gas volumes during lung inflation. MV can be avoided by using the 'INSURE' (INtubate-Surfactant-Extubate to CPAP) technique and this method has beenshown in randomized trials to reduce the need for MV and subsequent bronchopulmonary dysplasia (BPD)[15,16]. Following surfactant administration there may, after a variable period of time, be a need for a further dose of surfactant. In randomized trials 2 doses are better than a single dose[17] and a study with poractant alfa showed that up to 3 doses compared to a single dose reduced mortality (13 vs. 21%) and pulmonary air leaks (9 vs. 18%)[18]. It is practical to use a flexible dosing schedule basing the time of repeat doses on the baby's clinical condition and oxygen requirements and there are pharmacokinetic data to support this approach [19] Although clear evidence of long-term benefit is still lacking [20], tolerating higher $PaCO_2$ levels can lead to reduced time on MV and is now accepted practice [21]. Implementation of a ventilation weaning protocol allowing a degree of hypercarbia can result in earlier extubation and overall reduction in the duration of MV [22]. Several authors have reported low gestation to be a risk factor for poor responsiveness, while gender has not been reported by any. However, it has been shown that neonatal mortality, short-term morbidity and adverse neurodevelopmental outcomes are higher among male than female infants. In our study, PDA incidence was 86% which is much higher when compared to the study findings of Deniz *et al*.

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Conclusion

Early institution of CPAP in the management of RDS in premature neonates, can significantly reduce the need for MV & surfactant therapy. 50% babies of very preterm babies required no/minimum respiratory support of <24 hours Babies needing intubation before trial of CPAP, babies, preterm labor and with hsPDA are associated with long duration respiratory support. And also large scale Randomized controlled trials (RCTS) are warranted for further analysis of immediate and long term outcomes of CPAP and factors influencing those outcomes in neonates with RDS.

Source of support: None.

Conflict of interest: None.

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